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ÜBER WÄRMETHERAPIE BÖSARTIGER TUMOREN[1]

von

Kristian Overgaard

Herrn Prof. Dr. Vald. Henriques an seinem 70. Geburtstag gewidmet.

Sowohl aus älteren Zeiten als aus den letzteren Jahren liegen vereinzelte Mitteilungen über die Beobachtung einer spontanen Heilung bösartiger Geschwülste (vorwiegend Sarkome) im Anschluss an lange dauernde febrile Leiden bei dem tumortragenden Patienten vor. Diese Krankheitsbilder waren so auffallend, dass man auf Grundlage derselben die Gründung einer Therapie versucht hat, welche durch Hervorrufung eines derartigen febrilen Zustandes das Tumorleiden heilend beeinflussen können sollte.

Wenngleich diese Behandlungen bis jetzt nur wenig erfolgreich waren, liegen immerhin Beobachtungen vor, welche annehmen lassen, dass Möglichkeit dafür bestehe, durch Wärmebeeinflussung einen therapeutischen Effekt auf gewisse Geschwulstleiden zu üben.

Nachdem die Hochfrequenztechnik eine Höhe erreicht hatte, welche die Ausnutzung der Apparate für chirurgische Zwecke ermöglichte, wurden dieselben für Elektrokoagulation von Geschwülsten in Anwendung gebracht. Durch diese Behandlung wurde das von der Oberfläche aus zugängliche Geschwulstgewebe neben dem angrenzenden normalen Gewebe destruiert. Diese Methode findet fortwährend in weitem Umfange Verwendung. Sie bietet allerdings den Vorzug, dass Gefässe und Gewebsspalten verschlossen werden, ob sie sich aber hierüber hinaus von anderen die Entfernung des Tumorgewebes bezweckenden chirurgischen Eingriffen grundsätzlich unterscheidet, dürfte zweifelhaft sein.

Im starken Gegensatz zu dieser, eine primäre, ziemlich umgrenzte Gewebsdestruction bezweckenden »chirurgischen Diathermie» steht die »medizinische Diathermie», welche eine weit schwächer ausgesprochene

[1] Bei der Redaktion am 30. I. 1934 eingegangen.

(Aus der Radiumstation in Copenhagen. Chef: Dr. Med. J. Juul.)

Wärmebeeinflussung eines häufig grösseren Gewebsgebietes bezweckt. Dieses Verfahren wurde hauptsächlich bei entzündungsartigen Leiden in Anwendung gebracht, aber bereits zu einem frühen Zeitpunkt hat man dasselbe als Behandlung bösartiger Tumoren versucht (THEILHABER), angeblich mit einigem Erfolg. Die Resultate dieser therapeutischen Versuche waren indessen nicht überzeugend, und irgendwelche Verbreitung von Belang hat diese Therapie nicht gewonnen, was wesentlich dem Umstande zu verdanken sein dürfte, dass die sich zur betreffenden Zeit im reissenden Fortschritt begriffene Röntgenbehandlung sich derselben weit überlegen erwies. CHR. MÜLLER hebt jedoch hervor, dass er in gewissen Fällen eine Combination der beiden Behandlungsweisen besonders erfolgreich gefunden hat.

Dieser Diathermiebehandlung von Geschwulstgeweben liegt ein Gedanke zu Grunde, welcher zum Teil dem Gedanken entspricht, der den verschiedenen Versuchen zu Grunde lag, durch generelle Hyperpyrexie die Ausheilung eines Geschwulstleidens herbeizuführen, nämlich dass das Tumorgewebe Wärmebeeinflussung gegenüber weniger widerstandfähig sei als das angrenzende gesunde Gewebe.[1] Im einen Falle sucht man durch eine generelle Beeinflussung die Temperatur des ganzen Körpers derart zu steigern, dass die Tumorzellen getötet werden ohne dass die übrigen Zellen des Organismus zu Grunde gehen, im andern Falle sucht man dies durch eine locale Erwärmung des leidenden Abschnittes des Organismus zu erreichen.

Der ganze Sachverhalt ist indessen bis heute nur wenig erforscht, und genauere Untersuchungen hinsichtlich der Wärmeresistenz der verschiedenen normalen und pathologischen Gewebe des Organismus fehlen noch. Immerhin scheint aus den bereits jetzt vorliegenden Untersuchungen hervorzugehen, dass die verschiedenen Gewebe eine ziemlich variierende Toleranz aufweisen, und dass dieselbe zu einem gewissen Grade von der Wachstumsenergie des betr. Gewbes abhängig ist, so dass schnell wachsendes Gewebe leichter beeinflussbar ist als langsam wachsendes — eine ähnliche Erscheinung wie die sich in Bezug auf Strahlenempfindlichkeit geltend machende. Das spezifische Testisepithel scheint ganz besonders wärmeempfindlich. Die Untersuchungen erweisen ferner, dass nicht allein die absolute Temperatur, sondern auch die Dauer der Beeinflussung von ausschlaggebender Bedeutung ist.

Ebenfalls die Untersuchungen über die Wärmeempfindlichkeit transplantierbarer Tiertumoren in vitro sind wenig erschöpfend. Prof. C. O. JENSEN hat 1903 nachgewiesen, dass ein transplantierbares Rattensar-

[1] Auch die Möglichkeit einer cancericiden Wirkung verschiedener Toxine oder Nekrohormone ist in diesem Zusammenhang diskutiert worden; ebenfalls die Möglichkeit der Herbeiführung eines »Umstimmung» des Reactionsverhaltens des Organismus Tumoren gegenüber mittels Temperaturerhöhungen.

kom sein Anschlagsvermögen verlor, wenn es 5 Minuten hindurch einer Temperatur von 47° C ausgesetzt wurde; späterhin beobachteten STEVENSON und RODENBURG & PRIME,[1] dass selbst erheblich niedrigere Temperature bei länger dauernder Beeinflussung genügten um die Anschlagsfähigkeit von Tumorgewebe zu zerstören.

Trotz der Unvollständigkeit dieser Versuche scheint immerhin festzustehen, dass das Tumorgewebe eine etwas schwächere Wärmetoleranz aufweist als die meisten normalen Gewebe. Ebenfalls vereinzelte Untersuchungen über das Verhalten von Tumorgeweben und von verschiedenen normalen Geweben in Gewebskulturen scheinen dies zu bestätigen.

Versuche, einen überpflanzten Tumor (in vivo) mittels Diathermie einer Wärmebeeinflussung auszusetzen wurden von RODENBURG & PRIME vorgenommen. Die angewandte Technik gestattet indessen keine näheren Schlussfolgerungen bezüglich der betreffenden Wärmebeeinflussung selbst. Die einen bis mehrere Tage nach der Behandlung erfolgende histologische Untersuchung der Geschwülste zeigte eine starke Hyperämie, fehlende Mitosen im Gewebe und einen allmählig eintretenden Zerfall des Geschwulstgewebes, während das angrenzende Bindegewebe ungeschädigt schien. Untersuchungen über die Möglichkeit einer radicalen Ausheilung auf diesem Wege scheinen von diesen Forschern nicht vorgenommen worden zu sein. Die Versuche von LIEBSNY nach dieser Richtung hin gelangen ihm nicht, er hat nur zu konstatieren vermocht, dass eine Diathermiebehandlung überpflanzter Geschwülste deren Wachstumsenergie etwas herabsetzte.

WESTERMARK[2] hat die Untersuchung dieser Fragen in einer grösseren Arbeit (1927) aufgenommen. Seine Untersuchungen ergaben, dass es möglich war, Ratten, an welchen bösartige Geschwülste eingeimpft waren, durch eine Diathermiebehandlung, welche das angrenzende gesunde Gewebe unbeschädigt liess, zu heilen. Die benutzten Tumoren waren teils Flexner-Joblings Rattencarzinom, teils C. O. Jensens Rattensarkom. Aus seiner hübschen Versuchsaufstellung geht hervor, dass man durch eine locale Wärmebehandlung, bei Anwendung von Temperaturen um 44—48° C ein Tier von einem implantierten Tumor ohne Nekrose des normalen Gewebes heilen kann, wenn man mit der Behandlung hinreichend lange Zeit fortfährt, und dass zwischen der angewandten Temperatur und der erforderlichen Zeit ein gesetzgeregelter Zusammenhang besteht; diese Relation befolgt das Gesetz von ARRHENIUS. Die beanspruchte Wärmebeeinflussung variierte zwischen 48°/20′[3] und 44° /180′. Bei einer Temperatur niedriger als 44° blieb die Behandlung ohne nachhaltige Wirkung auf den Tumor. Die geringfügige Anzahl der mit-

[1] Arch. of Surgery 2, 1921.
[2] Skandinav. Archiv für Physiologie *52*, 1927.
[3] 48° C in 20 Minuten.

geteilten Versuche gestatten indessen kaum eine statistische Bearbeitung.

Ein Vergleich der für die Tumordestruction beanspruchten Wärmebeeinflussung mit dem von FUKUI[1] beobachteten Verhalten der Wärmeresistenz des Testisepithels ergab, dass sich das Tumorgewebe kräftiger von Wärme beeinflussen liess als das Testisepithel. Diese Erscheinung trat insbesondere bei den niedrigeren Temperaturen hervor. Insofern die gefundenen Werte allgemeine Gültigkeit besitzen, besagt dies, dass die Aussicht auf eine elective Tumordestruction durch eine derartige Behandlung bei den niedrigeren Temperaturen am grössten ist.

Die auf die Möglichkeit einer effectiven Wärmetherapie bösartiger Geschwülste kräftig deutenden Untersuchungen von WESTERMARK fanden bis jetzt nur wenige Beachtung. Dass die Therapie von denselben keine Spur trägt, dürfte zum Teil dem Umstande zu verdanken sein, dass die bisherigen technischen Hilfsmitteln die Anwendung einer derartigen Therapie auf Menschen nicht gestattete. Ebenfalls die soweit aus den Versuchen ersichtlich erforderliche Höhe der Temperatur mag abschreckend gewirkt haben. Noch die experimentelle Therapie hat aber die Frage einer Nachprüfung unterziehen lassen.

Da nun indessen diese Erscheinungen Aufmerksamkeit zu verdienen schienen, wurde im Sommer 1932 eine Reihe diesbezüglicher Untersuchungen in Angriff genommen u. z. mit weissen Mäusen als Versuchstiere. An den Schwänzen derselben wurden Tumoren implantiert. Man hat hauptsächlich mit Crocker mouse sarcoma 180 (»Woods Sarkom») gearbeitet.

Diese Geschwulst gibt in ungef. 98 % Anschlag; spontane Remission der entwickelten Tumoren kommt äusserst selten vor. Die Geschwulst metastasiert häufig nach Gl◌ndeln und nach parenchymatösen Organen (insbesondere Lunge und Leber). Bei Implantation am Körper tötet sie gewöhnlich die Tiere im Laufe von 6—8 Wochen, bei Implantation am Schwanz etwas später. Die Wärme- und Röntgenresistenz des Tumores in vitro wurde von RODENBURG & PRIME untersucht, und die betreffenden Untersuchungen ergaben, dass Temperaturen von 43° und hierüber auf den Tumor eine Wirkung üben. Die Geschwulst wächst ziemlich schnell und hat bereits ungef. 8 Tage nach der Implantation (bei Einimpfung am Schwanz) ungef. die Grösse eines Apfelsinkerns erreicht.

Wenn die Geschwulst eine dienliche Grösse erreicht hatte, wurde sie einer Diathermiebehandlung unterzogen. Hierfür wurde ein Funkenstrecke-Apparat älterer Konstruktion benutzt. In einigen Fällen wurde die eine Elektrode direct am Tumor und die andere an der Gegenseite des Schwanzes angelegt, so dass der Diathermiestrom das Tumorgewebe »in Serie» mit dem gesunden Gewebe durchquerte; in anderen Fällen

[1] Japan med. World *3*, 1923.

wurden beide Elektroden an der Seite des Tumors und des angrenzenden gesunden Gewebes angelegt, so dass der Strom die Gewebe »parallel» passierte. Irgendwelcher Unterschied war bei diesen beiden verschiedenen Anordnungen nicht nachweisbar. Die Temperatur im Inneren des Tumors wurde während der Behandlung durch Einführung einer kleinen Thermonadel gemessen. Die Durchwärmung hat eine Stromstärke von ungef. 20—50 M. amp. beansprucht, je nach Grösse der Elektroden und der erwünschten Höhe der Temperatur. Sämtliche Tiere wurden während der Behandlung mit Urethan narkotisiert. Die Temperatur des Gewebes erreichte in dieser Weise von 42°—46° und die Behandlungsdauer variierte zwischen 15 und 60 Min. In manchen Fällen wurde auch eine weniger kräftige Behandlung versucht, jedoch ohne nachhaltigen therapeutischen Effekt.

Gesunde Mauseschwänze, welche dieser Behandlung ausgesetzt wurden, wiesen gewöhnlich keine Reaction oder höchstens ein leichtes Röten und eine leichte Anschwellung der Behandlungsstelle auf. Eine derartige Reaction war gewöhnlich im Laufe einiger Tage vollständig abgeklungen. Verbrennungen wurden nur im Anschluss an technische Unfälle beobachtet.

Ganz anders stellten sich die Verhältnisse, wenn der Schwanz Sitz eines implantierten Tumors war. Die Versuche ergaben, dass es in einer Anzahl von Fällen bei der angewandten Technik möglich war, die Ausheilung desselben ohne Schädigung des angrenzenden (und peripheren) gesunden Gewebes herbeizuführen, d. h. *dass für eine elective Beeinflussung eines Tumores Möglichkeit besteht.* Die hiermit verknüpften Schwierigkeiten waren jedoch gross, u. z. hat es sich leichter erwiesen eine Destruction des Geschwulstgewebes zu erlangen als eine secundäre Zerstörung des angrenzenden gesunden Gewebes zu vermeiden.

Das unbehandelte Geschwulstgewebe wies gewöhnlich ein schwach rötliches, perlmutterartiges Schimmer auf und nahm sofort nach der Behandlung ein stark cyanotisches Aussehen an. Im Laufe der nächsten Tage nahm diese Misfärbung zu und im Laufe von 4—5 Tagen nekrotisierte das Geschwulstgewebe vollständig und an seinem Platze entstand eine Ulceration, welche bei grösseren Tumoren oft erheblich in die Tiefe gehen konnte, so dass der Knochen am Boden blossgelegt war. Das umgebende Gewebe wies bis zu diesem Zeitpunkt keine oder eine nur geringfügige Reaction auf (ein wenig Röte und Anschwellung), während der distale Abschnitt des Schwanzes ein natürliches Aussehen hatte. Nach Auftreten der Ulceration änderten sich die Verhältnisse erheblich: In einer sehr grossen Anzahl der Fälle stellten sich ringsum die Ulceration secundäre inflammatorische Vorgänge ein, welche in vielen Fällen auf die Gefässe übergriffen und dadurch eine Kompromittierung der Ernährung des peripheren Schwanzabschnittes verursachten. Das Gewebe

wurde hier cyanotisch und ödematös, und in den Fällen wo derartige Schädigungen eintraten, ging der periphere Abschnitt gewöhnlich zu Grunde und wurde abgestossen, so dass der Schwanz am Sitze des Tumors spontan amputiert wurde. Alle die betreffenden Versuche wurden ausgeschaltet. Der zurückgebliebene Schwanzstümmel wies selbst nach mehrmonatlicher Observation meistens keine Recidivanzeichen auf. Dass diese Störung der Ernährungsverhältnisse dem Auftreten der Ulceration und nicht einer Spätwirkung der Behandlung auf das normale Gewebe zu verdanken war, lässt sich aus der Tatsache erkennen, dass Kontrolltiere, deren Schwänze einer ähnlichen oder noch kräftigeren Behandlung ausgesetzt wurden, keine entsprechende Reaction aufwiesen, und ferner dass eine solche nicht in denjenigen Fällen auftrat, wo die Tumorinfiltration eine weniger tiefgehende und die Ulcerationsbildung deshalb eine mehr oberflächliche war.

Ein beträchtliche Anzahl der vorgenommenen Versuche wurden durch diesen Umstand vereitelt. In anderen Versuchen gelang es aber, eine Schädigung der peripheren Schwanzteile zu vermeiden. In diesen Fällen reinigte sich der Defekt und wurde allmählig von Epithel bekleidet, welches vom Rande aus nach innen wuchs. Die hierfür beanspruchte Zeit war von der Grösse des Tumors abhängig. Falls dieser so tief ging, dass das Knochengewebe blossgelegt wurde, stellten sich ostitische Vorgänge in demselben ein, bei Ausstossen von Sequestern (mitunter einer oder mehrere der Schwanzwirbeln), was oft eine knickförmige Deformierung des Schwanzes zur Folge hatte. — In solchen Fällen beanspruchte das Heilen oft gegen ein paar Monate, bei weniger tiefgehenden Defekten mitunter nur ein paar Wochen. Auch nach mehr oberflächlichen Defekten konnten durch Schrumpfen des Narbegewebes Knickbildungen des Schwanzes entstehen. Bei tiefergehenden Tumoren zeigte sich nach der Ausheilung stets ein deutlicher, dem von der Geschwulst destruierten Abschnitt entsprechender Defekt; oberflächliche Tumoren hinterliessen meistens nur eine glatte in natürlichen Niveau liegende Cicatrice.

Durch eine genügend kräftige Wärmebehandlung liess sich in sämtlichen Fällen eine deutliche Wirkung auf das Tumorgewebe herbeiführen. Ebenfalls nach einer schwächeren Beeinflussung wies dasselbe durchgängig eine deutliche Reaction auf (Hyperämie oder mehr oder weniger oberflächliche Ulceration), ziemlich kurz nach der Behandlung stellte sich aber wiederum Wachstum des Geschwulstgewebes ein u. z. meistens aus den Rändern der ursprünglichen Geschwulst. Dies konnte auch in Erscheinung treten, wo die Technik versagt hatte, z. B. bei ungenügender Adaptation der Electroden. Die Behandlung der Tumoren erfolgte auf einer derart frühen Stufe, dass dieselben noch keine Metastasen gebildet hatten; nur in einem einzelnen Fall, wo das Tier ungef. 2 Monate nach der Behandlung starb, wurden in den Lungen zahlreiche

Metastasen vorgefunden, während am Platze des ursprünglichen Tumors kein Geschwulstgewebe nachweisbar war.

In mehreren Fällen wurden die histologischen Veränderungen des wärmebehandelten Geschwulstgewebes untersucht. Sowohl die Behandlungstemperatur als die Behandlungsdauer wurden in verschiedenen Serien variiert, u. z. derart dass einige der Geschwulste nur einer relativ schwachen (subtherapeutischen), andere dagegen einer ziemlich gewiss geschwulsttötenden Wärmebeeinflussung ausgesetzt wurden. Es wurden Serien mit 42°/5′, 42°/30′, 46.5°/5′, 46.5°/10′, 46.5°/20′ und 46.5°/30′ behandelt. Innerhalb dieser Serien wurden Tiere zwecks Untersuchung 0, 5, 15, 30, 45 Minuten, 1, 2, 3, 6, 14 Stunden und 1 ×, 2 ×, 3 × 24 Stunden nach erfolgter Wärmebehandlung getötet.

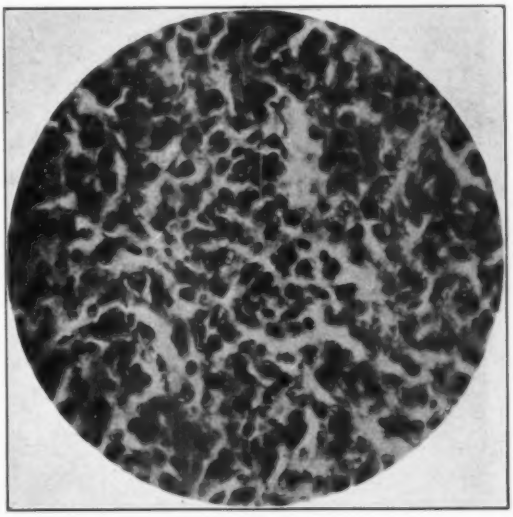

Fig. 1. Unbehandeltes Geschwulstgewebe. Zahlreiche Gefässe, aber keine mit sichtbarem Blutinhalt, Geschwulstzellen mit feinem Chromatinnetz. Zellgrenzen undeutlich.

Im nicht-behandelten Geschwulstgewebe (Fig. 1) begegnen uns ziemlich zahlreiche aber nur wenig bluthältige Gefässe, während sich das wärmebehandelte Geschwulstgewebe in starkem Gegensatz hierzu stets stark hyperämisch erwies. So war bereits bei Beendigung der Behandlung eine starke Blutanhäufung in den Gefässen wahrnehmbar (Fig. 2), und diese Hyperämie nahm im Laufe der folgenden Stunden zu und war 6—24 Stunden nach der Behandlung am kräftigsten ausgesprochen. Zu diesem Zeitpunkt begegnen uns auch häufig kleine Blutungen im Geschwulstgewebe. Diese Hyperämie scheint innerhalb der untersuchten Rahmen von der Höhe der Wärmebeeinflussung nicht abhängig zu sein. Ebenfalls das im betreffenden Bereich liegende gesunde Gewebe wies etwas Hyperämie auf, allerdings aber meistens nicht so hochgradig wie diejenige des Geschwulstgewebes.

Ausser der Hyperämie wies das Geschwulstgewebe bei Beendigung der Behandlung bzw. eine kürzere Zeit danach keine deutliche Veränderung auf. Die Structur der Geschwulstzellen schien eine natürliche zu

sein. In den kräftig beeinflussten Serien wurden einige Zeit nach der Behandlung kennbare Veränderungen wahrgenommen: Die Kerne der Geschwulstzellen verloren ihre feine Chromatinstructur, sie schrumpften und wurden gleichartig dunkel färbbar, mitunter ungleichmässig kleinknotig. Zahlreiche Zellen (Fig. 3) wiesen ein etwas dunkleres, feinkörniges Protoplasma auf, wodurch die unter normalen Verhältnissen sehr undeutlichen Zellengrenzen scharf hervortraten. Diese Veränderungen waren durchgängig 24 Stunden nach der Behandlung ausgesprochen, am häufigsten aber bereits 3—6 Stunden nach derselben verspürbar. Bei Untersuchung 2 und 3×24 Stunden nach der Behandlung erwiesen sich diese Zerfallvorgänge, von einer stark ausgesprochenen Karyorrhexis und Karyolysis begleitet, noch weiter fortgeschritten, und der Zellenzerfall war meistens derart ausgesprochen, dass die ursprüngliche Structur des Gewebes beinahe verwischt war. Im angrenzenden gesunden Gewebe begegneten uns durchgängig eine Anzahl Leukocyten und Fibroblasten, welche häufig nach dem zerfallenden Tumor hin eine deutliche Demarkationszone bildeten. Auch das Geschwulstgewebe selbst wies auf diesen Stufen häufig eine Anzahl Leukozyten auf.

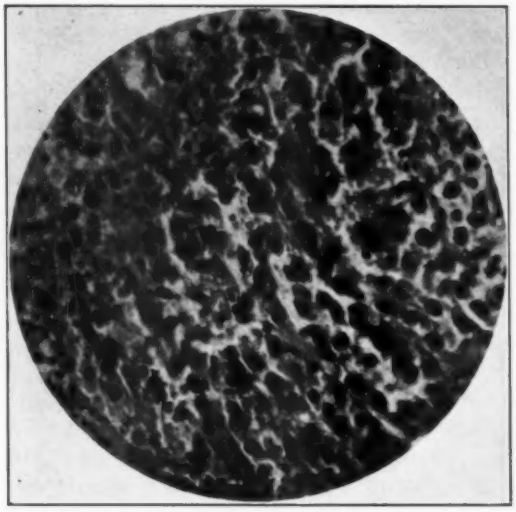

Fig. 2. Geschwulstgewebe 5 Minuten nach der Beendigung der Behandlung. Starke Blutfüllung der zahlreichen Gefässe. Die Geschwulstzellen sind im übrigen unverändert.

Ähnliche, aber weniger ausgesprochene Veränderungen waren auch in einigen der mit kleineren Dosen ($42°/5'$ und $46.5°/5'$) behandelten Geschwulsten wahrnehmbar; hier begegnete uns aber neben den stark zerfallenen auch eine Anzahl wenig geschädigter Zellen u. z. insbesondere in den tieferen Abschnitten des Geschwulstgewebes. Meistens wurde hier keine Demarkationszone beobachtet.

Das unbehandelt gebliebene Geschwulstgewebe enthielt eine erhebliche Anzahl Mitosen. Im gesamten behandelten Geschwulstgewebe war die Anzahl derselben einige Zeit nach der Behandlung bedeutend herab-

gesetzt, und im kräftiger beeinflussten Geschwulstgewebe begegneten uns 24 Stunden nach der Behandlung und später keine Mitosen.

Das benachbarte gesunde Gewebe wies kurz nach der Behandlung etwas Hyperämie auf, späterhin zeigten sich am Rande gegen Tumor hin reichliches Granulationsgewebe und eine Anzahl Leukozyten; hierüber hinaus aber wurden hier keine pathologischen Veränderungen wahrgenommen. Nur die Haut direct über den Gipfel des Tumors wies häufig starkes Ödem und Anzeichen von Zerfall auf. Da ähnliche Veränderungen am Platze der anderen Electrode nicht beobachtet wurden, muss angenommen werden, dass die betreffenden Veränderungen zum Teil durch den Druck des Tumors hervorgerufenen Ernährungsstörungen zu verdanken sind.

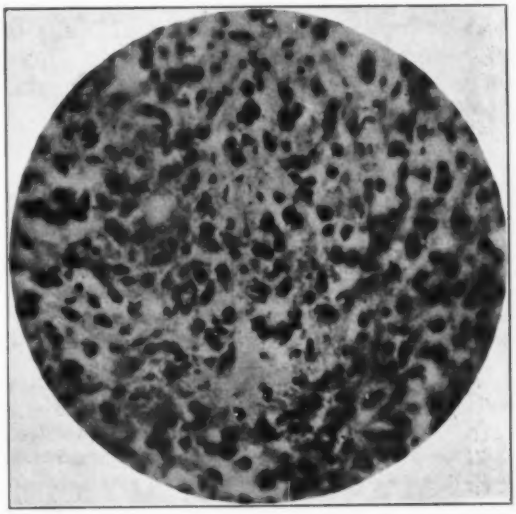

Fig. 3. Geschwulstgewebe 24 Stunden nach der Behandlung. Sehr starke Blutfüllung mit weit dilatierten, bluthaltigen Gefässen. Blutungen im Gewebe. Die Geschwulstzellen stark zerstört. Die Kerne eingeschrumpft und dunkelfarbig. Zusammenballung der Chromatinsubstanz. In einigen Zellen beginnende Chromatolyse. Das Protoplasma dunkel und feinkörnig, deutlich abgegrenzt ringsum die Kerne. Keine Mitosen.

Eine postmortelle Untersuchung der ausgeheilten Mäuse deckte am Platze des Tumors ein fibröses von einer dünnen unbehaarten Hautschicht überdecktes Narbegewebe auf.

In welcher Weise die Wärme das Geschwulstgewebe destruierend beeinflusst, bleibt noch unerläutert. Aus den histologischen Untersuchungen ergibt sich, dass von einer eigentlichen Wärmecoagulation nicht die Rede ist. WESTERMARK meint aus seinen Versuchen schliessen zu dürfen, dass es sich um eine durch die Wärme bedingte Zerstörung gewisser Fermente der Geschwulstzelle handelt. In einer Anzahl der hier vorliegenden Versuche wurde jedoch eine nachhaltige Wirkung auf das Geschwulstgewebe durch Wärmebeeinflussungen constatiert, welche laut Angabe von WESTERMARK derart geringfügig sind, dass sie das betreffende Ferment nicht kennbar zu beeinflussen vermögen sollten.

Protokol-Nr.	Datum der Behandlung	Grösse der Geschwulst (Drei Dimensionen in mm)	Wärmebeeinflussung (° C/min.)[1]	Lokale Dauerheilung			Observationszeit (in Tagen)	Metastasen
				mit tiefem (knöchernen) Defekt	mit oberflächlichem Defekt	one sichtbares Defekt		
7 . .	25/5 32	17 · 6 · 7	46°/5 + 60′	+			372	÷
12 . .	26/5 32	13 · 7 · 5	46°/7 + 30′	+			63	÷
37 . .	4/6 32	9 · 3 · 2	45°/5 + 30′	+			404	÷
48 . .	7/6 32	17 · 3 · 2	45°/12 + 20′	+			294	÷
63 . .	13/6 32	reiskorngross	42°/13 + 30′		+		150	÷
76 . .	22/6 32	7 · 3 · 2	45°/2 + 35′			+	381	÷
90[2] . .	28/6 32	2 Geschwülste, reiskorngross	46°/4 + 20′			+	56	+
	(28/7 32)		(46°/10 + 20′)			(+)	(26)	
99 . .	4/8 32	9 · 4 · 5	45.5°/5 + 30′		+		176	÷
106 . .	8/8 32	Wurstähnlich, fast um das ganze Circumferenz in einer Länge von 9 mm.	44°/5 + 25′			+	232	÷
128 . .	23/8 32	13 · 4 · 3	46°/5 + 30′		+		240	÷
161 . .	8/9 32	12 · 4 · 3	45°/5 + 25′		+		413	÷
165 . .	10/9 32	9 · 4 · 3	45°/4 + 30′		+		436	÷
166 . .	10/9 32	12 · 4 · 4	45°/5 + 30′			+	199	÷
171 . .	14/9 32	18 · 4 · 3	46°/5 + 20′			+	196	÷
202 . .	29/9 32	11 · 4 · 3	43°/5 + 20′		+		357	÷
223 . .	5/10 32	7 · 3 · 3	43°/3 + 20′			+	314	÷
225 . .	9/10 32	17 · 3 · 1.5	42°/5 + 30′			+	60	÷
226 . .	6/10 32	11 · 3 · 3	42°/6 + 20′			+	173	÷
229 . .	7/10 32	10 · 3 · 2	43°/5 + 30′			+	60	÷
262[3] . .	8/11 32	11 · 3 · 3 3 · 2 · 2	43°/5 + 20′		+		400	÷
263 . .	8/11 32	7 · 3 · 3	42°/5 + 30′			+	153	÷
264 . .	8/11 32	11 · 4 · 3	42°/5 + 30′			+	274	÷

Verschiedene Untersuchungen über die Wärmeempfindlichkeit von Gewebskulturen und niedrigeren Organismen deuten darauf hin, dass hier von einer Reaction die Rede ist, welche bei leichterer Beeinflussung

[1] Zähler: Behandlungstemperatur in °C.
Nänner: Erste Zahl: Zeit bis die erwünschte Temperatur erreicht ist.
Zweite Zahl: Eigentliche Behandlungszeit.

[2] Nach einem Monat Recidiv in der distalen Geschwulst. Wiederholte Diathermie 46°/10 + 20′. Glatte Heilung. Bei der Sektion wurde kein lokales Recidiv aber pulmonale Metastasen gefunden.

[3] 2 Geschwülste.

reversibel ist, bei kräftigerer Beeinflussung aber stationär wird. Dass der hochfrequente Strom an sich (bei den hier benutzten Frequenzen) auf das Geschwulstgewebe irgend welche spezifische Wirkung ausüben sollte, dürfte ebenfalls ausgeschlossen sein.

Nachstehend sind einige Versuchsprotokolle skematisch verzeichnet. Nur solche Versuche, wo die gestellte Aufgabe: Ausheilung des Geschwulstleidens ohne Schädigung des benachbarten Gewebes gelungen ist, wurden mitgenommen. Im grossen Ganzen bewähren diese Versuche die Versuchsergebnisse von WESTERMARK. Immerhin ist beobachtet worden, dass sich die beabsichtige Wirkung unter den vorliegenden Verhältnissen durch Anwendung teils niedrigerer Temperature teils einer kürzeren Behandlungsdauer erreichen liess, als in seinen Versuchen möglich schien.

ZUSAMMENFASSUNG

Die vorgenommenen orientierenden Untersuchungen erweisen, dass die Ausheilung einer implantierten Geschwulst (Woods Sarkom) durch eine relativ geringfügige Wärmebeeinflussung bei Mäusen möglich ist. Das Geschwulstgewebe wird hierdurch erheblich stärker geschädigt als das benachbarte gesunde Gewebe, d. h., *dass eine derartige Beeinflussung electiv geschwulsttötend ist.*

Diathermiebehandelte Geschwulstgewebe weist im Gegensatz zum gesunden Gewebe eine characteristische, sich in Gestalt von Hyperämie des Geschwulstgewebes und Zerfall der Geschwulstzellen Ausdruck gebende Reaction auf.

Frühere diesbezügliche Untersuchungen haben in grossen Zügen ihre Bestätigung gefunden. Immerhin erscheint es möglich, durch eine erheblich kleinere Wärmebeeinflussung als bisher angenommen, die Ausheilung eines Geschwulstleidens zu erreichen.

SUMMARY

These investigations prove that it is possible to obtain complete healing of an innoculated tumor (Woods Sarcoma) in mice by means of the influence of a relatively small amount of heat. The tumor is considerably more injured than the neighboring healthy tissue which means that *the effect produced in this way is elective and lethal for tumor tissue.*

In contrast to normal tissue, when treated by diathermy tumor tissue shows a characteristic reaction in the form of hyperemia and destruction of tumor cells.

Earlier investigations in this field have on the whole been verified. It still appears possible to attain complete cure of a tumor by the use of considerably less heat than has so far been used.

RÉSUMÉ

Les recherches orientatrices qui ont été faites montrent qu'il est possible de guérir, par une action calorique relativement faible, une tumeur (sarcome de Wood) greffée à des souris. Le tissu néoplasique se trouve ainsi notablement plus atteint que les tissus

sains environnants, c.-à.-d. *qu'une action de cette nature est électivement mortel pour le néoplasme.*

Contrairement aux tissus sains, les tissus néoplasiques traités par la diathermie présentent une réaction s'exprimant par une hyperémie du tissu avec dégénération des cellules néoplasiques.

Les recherches antérieurement effectuées sur ce sujet ont, dans leurs grandes lignes, trouvé leur confirmation. Toujours est-il qu'il paraît possible d'obtenir la guérison de néoplasme par des actions caloriques notablement plus faibles qu'on ne le croyait jusqu'ici.

THE SIMULTANEOUS RECORDING OF CARDIAC MOVEMENTS AND SOUNDS BY THE ROENTGEN RAY[1]

(Kymophonoroentgenography)

by

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and

Myron Schwarzschild, M. A.
Physicist

(Tabula XVI)

In studying the details of the roentgenkymographic waves made by the multiple slit method (STUMPF), several notches or serrations were noted, grafted on the main limbs of the waves. Three of these appear in almost all records in definite positions. One bears a rather definite relation to ventricular systole. It is a notch or a superimposed narrow peak on the ventricular waves approximately synchronous (within $^1/_{10}$ second) with systole as shown by the beginning outward thrust of the vascular waves (aorta and pulmonary arteries). This notch may be found on the ventricular wave either just preceding, at, or more often slightly after the beginning of the systolic limb.

There is a second serration on the ventricular wave which corresponds exactly in time with a notch on the retracting limb of the vascular waves (aorta and pulmonary artery). This serration usually has the form of a steplike interruption to the smooth progress of the diastolic limb of the ventricular wave within one tenth second of its onset.

The third serration has the appearance of a more or less steep incisure on the descending limb of the vascular waves (aorta and pulmonary artery). It occurs about $^1/_5$ second after the maximum outward thrust of the vessels.

[1] Submitted for publication Jan. 10th, 1934.

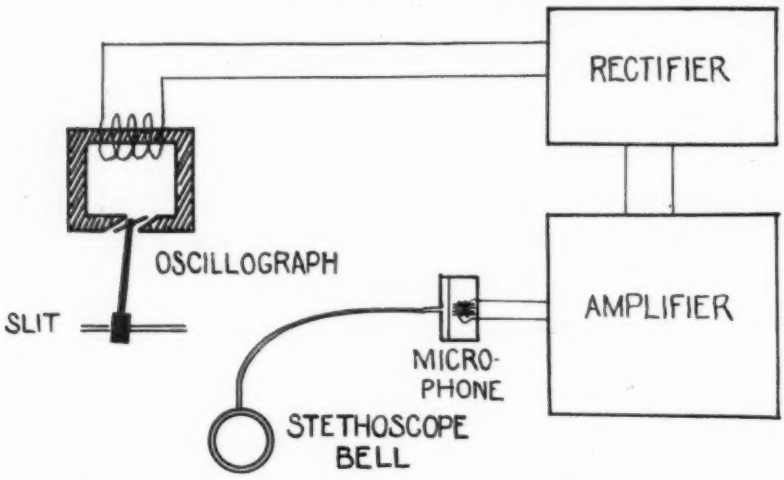

Fig. 3. Diagrammatic representation of the heart sound recording system.

These serrations represent actual motion of the ventricular wall and the vessel wall, vibrations extremely rapid, but nevertheless definite and clear cut. From the time relationships described above, it seemed highly probable that the notches were related to the valve action. Since the valve action is evidenced clinically by cardiac sounds, it appeared to us that the correlation of these serrations with sound records would establish their exact significance. Though of great interest, the problem of such correlation presented no little complexity.

To be of value the two phenomena were to be recorded simultaneously in such a way that the time scales on both could be readily compared. The simplest method of accomplishing this appeared to be, to record both the sound and the movement with the same roentgen beam on the same film or on different films moving together. The plan in essence then, was to cause the heart sounds to move a lever, opaque to roentgen-rays, bearing the same relation to a slit and film, as does the heart in the kymographic procedure. By making the slit for the recording of the heart sound, of the same width as the slits of the kymograph, the same degree of time resolution would be obtained, thus excluding the possibility of drawing unwarranted conclusions.

Our kymograms were made with a grid of essentially the same dimensions as that of STUMPF, but with a more rapid film motion. In this way a considerably greater time resolution is obtained and the notches which are of very short duration, are clearly outlined. The time resolution is

such, that an accuracy of time measurement of the order of 0.03 of a second is obtainable. This means that motions taking place within this time limit will not be recorded clearly, but phenomena extending over a period longer than 0.03 of a second will be discernible. The vibrations composing the heart sounds are of a duration of the order of magnitude of 0.005 seconds, corresponding to a frequency of about a 100 cycles per second. If the lever of the heart sound recording arrangement therefore had been made to move in front of the slit, with a motion corresponding to the sound vibrations themselves, no record of such motion would have been obtained. Furthermore since such a lever must possess considerable mass in order to be opaque to the roentgen-ray, a very high power would be necessary to drive it at the sound frequency. Fortunately both these limitations lie in the same direction and a simple solution to the problem was found.

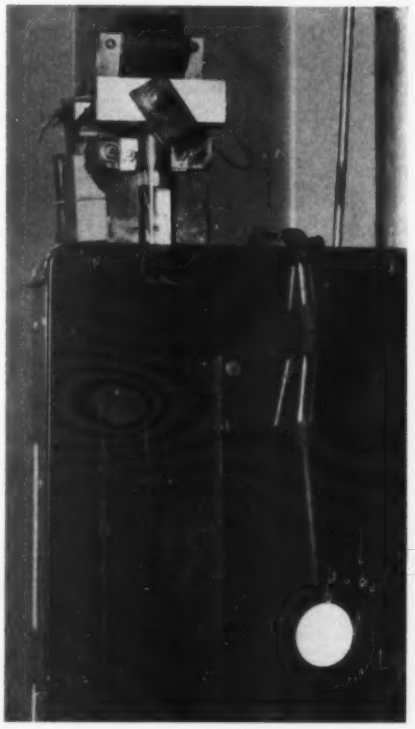

Fig. 4. Photograph showing oscillograph mounted in upper left hand corner of the kymographic apparatus and the stethoscope bell with which the sounds are picked up.

The heart sounds are picked up from the chest wall by means of a stethoscope bell made up of material transparent to the roentgen-ray and strapped to the patient. The sounds are carried through a rubber tube into a microphone, the output of which is connected to a multi-stage vacuum tube amplifier. In this amplifier electrical impulses from the microphone, corresponding to the frequency of the sounds are magnified. The output of this amplifier is then led into a rectifying system and from there to the coils of an electromagnet. This, when activated, attracts an iron armature so as to rotate an aluminium lever. To the end of this lever is attached a small piece of lead which moves in oil in front of a slit in a lead plate. Behind this plate is a cassette containing the roentgen film and intensifying screen mounted on a carriage which is firmly connected to the film carrier of the kymograph and moves with it.

The lever is thus actuated not by electrical impulses of the frequency of the heart sounds, but rather by electrical pulses, the duration of which corresponds to the entire duration of the sound and the intensity of which corresponds to the intensity of the second. At each heart sound the armature is attracted and the lead marker deflected in front of the slit, to return again at the end of that sound to its original position.

With this method of recording, an accuracy of measurement of the beginning and duration of the sounds to within 0.03 of a second is easily obtained. Since this is the limit of accuracy of the kymogram, nothing would have been gained as far as correlation is concerned, by using a more elaborate method of recording the sound.

Two major difficulties were encountered due to the effect of the operation of the roentgen-ray machine upon the sensitive heart sound apparatus. One source of interference came from the loud noise from the mechanical rectifier of the roentgen-ray machine. This effect was in great measure avoided by making the amplifier insensitive to high frequency sounds of which this noise is mainly composed, but this method of elimination leads to distortion and is never entirely satisfactory. The use of a valve tube machine, however, eliminates the noise completely. A second source of interference is electromagnetic in character and arises from two sources. First there is the effect of the stray magnetic field from the roentgen-ray transformer, which induces alternating currents in the amplifier. This was avoided by using very heavily shielded transformers and a very heavily shielded microphone and was completely eliminated by careful placement of the microphone and amplifier with

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Plate I.

Fig. 1. Left border of cardiac shadow showing kymographic waves. The waves over the aortic and pulmonary artery areas show the characteristic notching at a point on the retracting limb of the wave soon after its peak. Over the ventricular portion of the cardiac shadow the waves show a less prominent notch just beyond the point of beginning systole.

Fig. 2. Left border of cardiac shadow showing kymographic waves. Just after the point of beginning ventricular systole (peak of wave) may be seen the indentation corresponding to the first sound while the small ridge on the diastolic limb — (deepest point of valley of the wave) corresponds to the second sound.

Fig. 5. Heart sound records of five normal hearts. The shadow of the oscillograph when not in motion has straight edges. When actuated by the cardiac sounds, the peaks (the white peak and its corresponding black indentation) are produced. Record 2 shows prolonged sounds. Record 5 shows a reduplicated second sound. In record 3, the first sound is louder than the second while in record 4 the second sound is louder than the first. The time axis runs from below upward.

Fig. 6. A heart sound record is placed within a band bearing ventricular waves for purposes of correlation. + indicates the position of the microphone. In the same way, the sound record is placed in a band bearing aortic or pulmonary waves when correlation with these is desired.

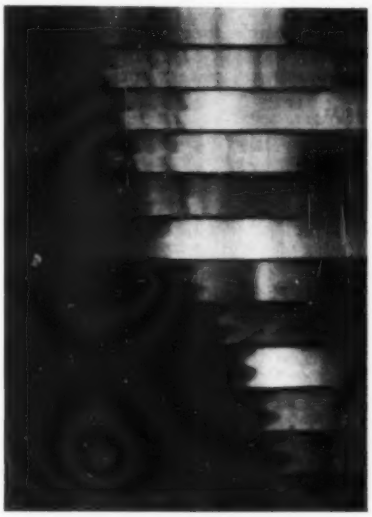

Fig. 1.

Fig. 2.

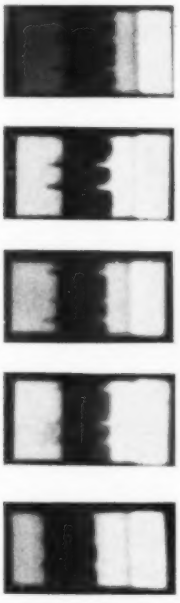

Fig. 5.

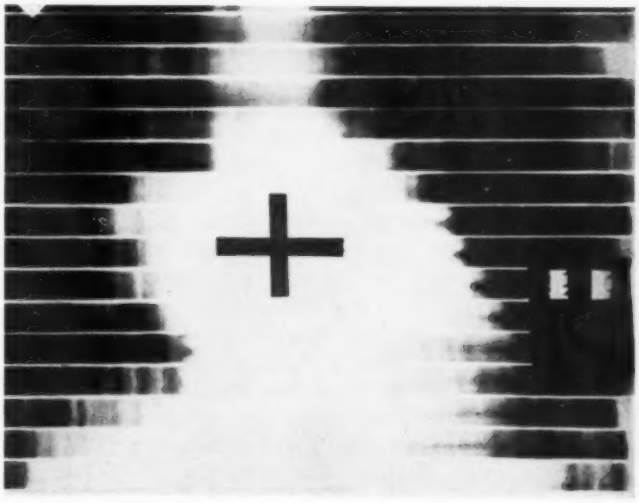

Fig. 6.

respect to the roentgen-ray transformer. Second, there is the effect of the heavy current drain of the roentgen-ray machine, which produces a small alternating component in the potential of the ground leads. This was eliminated entirely, by complete electrical shielding of the entire equipment and its use without a ground.

The developed sound film shows the record of the movement of the lead marker. In the absence of sound, the shadow of the marker is a straight bar with parallel sides, while with sounds, this shadow shows a notched edge. The depth of the notch varies with the intensity of the heart sound and the time of duration of the notch corresponds with the duration of the heart sound.

These shadow sound records have precisely the same time scale as the kymogram with which they are made, because the film for the sound record and that for the kymogram move together and the exposure of both films is made by the same roentgen-ray beam under the same conditions of excitation.

These sound records may be placed within a band of the kymogram and the relationship of the heart sound records and the phenomena depicted in the kymogram may be directly observed, or the waves may be compared by measurement with dividers.

Measurements so made show the following relationships. The first heart sound is simultaneous with the first notch on the ventricular wave which occurs within $^1/_{20}$ of a second of the peak of the wave, indicating a very rapid and small movement of the ventricular wall. The second sound is simultaneous with the notch, corresponding to the beginning of ventricular diastole and also with the indentation on the descending limb of the vascular waves (aorta and pulmonary artery).

It would appear that the notches on the kymographic waves of the heart are due to the hydro-dynamic action associated with the closure of the valves. It is unlikely that any muscular action of the chamber or vessel walls can account for such rapid and sharp motions, but it is very likely that these rapid motions are due to the reflection in the position of the walls, of sudden changes in pressure in the blood due to the closure of valves. Since our records show that the sounds are simultaneous with these notches to within 0.03 of a second, our time resolution, it must be concluded that certainly less than 0.03 of a second of the duration of a sound is attributable to causes other than valve action.

Our sound recorder, records only audible sounds and is very insensitive to slow subsonic vibrations. There is of course, therefore, the possibility that such vibrations may precede the first audible sounds and be due to the motion of the muscle itself. Such vibrations however, while they have been reported by others, are probably not sound and do not vitiate our conclusions.

This interpretation of the notching as far as the aortic wave is concerned is in complete agreement with experiments performed on animals by WIGGERS and others, who found an incisura on the descending limb of the aortic pressure curve corresponding to the closure of the semilunar valves and to the second sound. In fact the correlation is so good that we are tempted to consider the aortic waves on the kymogram, as being true pressure curves of the aorta, on an arbitrary pressure scale. Thus the kymogram would seem to provide the first means of securing aortic pressure curves in humans.

The method of recording heart sounds here described is of course applicable to any problem in which high frequency vibrations are to be recorded by means of an oscillograph of a relatively low natural period.

SUMMARY

The significance of notches on the aortic and the ventricular waves of the roentgen kymogram of the heart was investigated by making a roentgenkymogram of a lever whose movement represented the actual sound of the heart transmitted through a stethoscope of special construction and transformed by audion tubes and a special circuit.

These phonokymographic records were then checked against the serrations on the kymographic waves of the heart. They were found to correspond exactly. Thus it may be stated that the roentgenkymogram not only records the usually known movements of the heart, but also the movement phenomena associated with the production of the heart sounds.

ZUSAMMENFASSUNG

Die Bedeutung der Kerben an der Aorta-und den Kammerkurven des Röntgenkymogramms vom Herzen wurde untersucht, indem man Röntgenkymogramme eines Hebels machte, dessen Bewegung das wirkliche Herzgeräuch darstellte, das durch ein Stethoskop von spezieller Konstruktion übertragen und durch Audionröhren und einen speziellen Stromkreis transformiert wurde.

Diese phonokymographischen Aufzeichnungen wurden dann mit den Einkerbungen der kymographischen Herzkurven kollationiert. Es zeigte sich, dass sie einander genau entsprachen. Man kann also sagen, dass das Röntgenkymogramm nicht nur die gewöhnlichen bekannten Herzbewegungen aufzeichnet, sondern auch die mit der Erzeugung der Herztöne verbundenen Bewegungsphänomene.

RÉSUMÉ

L'auteur a procédé à l'étude de la signification des encoches des ondes aortique et ventriculaire des radiokymogrammes du cœur en prenant un radiokymogramme d'un levier dont le mouvement représente le son actuel du cœur transmis par un stéthoscope de construction spéciale et transformé par une lampe audion et un circuit spécial.

Ces résultats phonokymographiques sont ensuite reportés sur les dentelures des ondes kymographiques du cœur. La concordance était complète. Il est ainsi établi que le radiokymogramme ne donne pas seulement l'enregistrement des mouvements notoires du cœur, mais aussi celui des phénomènes moteurs associés à la production des bruits cardiaques.

FROM THE ROENTGEN DEPARTMENT OF ST. ERIK'S HOSPITAL, STOCKHOLM.
CHIEF: DR. CARL SANDSTRÖM

RÖNTGENKYMOGRAPHY AD MODUM STUMPF AS A METHOD OF EXAMINING THE HEART[1]

by

Bengt Ihre

(Tabulæ XVII—XIX)

Our ability to distinguish the finer details of cardiac movements by fluoroscopy is very limited. The different perceptions follow one another so closely that they are more or less completely fused and only the coarsest movements are grasped. A detailed study is possible only with the help of röntgenographic methods. There are available two methods of procedure, the cinematographic and the kymographic, which differ from one another somewhat in principle.

The cinematographic method requires no further explanation. It is a filming of the heart movements which may be carried out directly or indirectly. The latter alternative consists in taking a film of the fluoroscopic picture and seems to be of minor significance in studying cardiac movements. The most important röntgenographic studies of the heart are undoubtedly those of the GROEDEL brothers who made electrocardiograms at the same time as the film was being taken. Their experiments were prematurely interrupted by the outbreak of the world war but they had already had time to make several interesting observations. During recent years the GROEDEL apparatus has been considerably improved without anyone, however, being tempted to continue their experiments in earnest. This probably depended in part on the expense of the enormous quantity of film required and on the not inconsiderable risk of röntgen injury. Very recently JANKER and GOTTHEINER-JACOBSOHN have constructed apparatuses, with which very inexpensive filming of the heart can be done without danger of radiation, and in May 1932 JANKER and SCHMITZ even demonstrated a cardiac sound-film. Röntgen-

[1] Submitted for publication Jan. 16th, 1934.
A résumé of this paper was delivered before the Congress of the Northern Association for Medical Radiology, Stockholm, July 1933.

cinematography of the heart has, however, not yet acquired any greater practical significance.

Well developed röntgen cinematography could naturally be of extraordinary help in medical teaching. At present however it is difficult to imagine that the method could become of more general clinical diagnostic importance. The costs are too great and the results are too slight. In cinematography each exposure is represented by a separate film, while in kymography one single film records the result of a series of exposures. This latter fact of course greatly facilitates an accurate comparison.

The kymographic method of procedure is especially different from the cinematographic in that it is a continuous registration of movement. In its original and simplest form the kymographic apparatus consists of a metal disc, which is placed between the patient and the film kasette and has one or more narrow slit-like openings. If during exposure the kasette or the metal disc are moved at right angles to the slits, a continuous registration of movement is obtained. Moving the kasette or the metal discs thus prevents the pictures of the different phases of movement from covering one another. SABATT, GOETT and ROSENTHAL were probably the first who worked according to this principle (1912). In Sweden STENSTRÖM and WESTERMARK (1926) and SUNDBERG (1928) published interesting röntgen-kymographic experiments in which they took electrocardiograms and kymograms simultaneously.

All the earlier kymogram experiments were carried out with one or very few slit openings so that only movements in separate sections of the heart shadow could be studied. No comprehensive survey of the entire heart shadow has been obtained. The kymograph constructed by STUMPF in München is undoubtedly an improvement in this respect (Fig. 1). The metal disc has been replaced by a lattice or grid of parallel lead lamellae of exactly the same width (11.5 mm.) and separated by narrow slit-shaped openings (0.5 mm.). By means of a small attachment on the lower part of the kymograph, either the grid or the kasette during exposure are moved at right angles to the slit openings exactly the distance between two slits (12 mm.). The large number of slits makes it possible to obtain a general view of the heart shadow in its entirety. The velocity of the grid or of the kasette can be varied from 1 to 60 seconds by means of a timer. As exposure can only take place while the grid or the kasette is moving, it is practical to add an attachment to the kymograph by means of which the current to the röntgen tube is turned off and on automatically while the grid is moving.

The STUMPF kymograph, which in recent years has come more and more into use in the German clinics and abroad, is obtainable in two sizes. The *smaller* of these can be attached to a usual upright fluoroscopic stand without any special arrangements, while the *larger* requires

a specially constructed stand. The small kymograph allows a registration only with the slits running horizontally. The larger is on the other hand rotatable, thus permitting an optional adjustment of the slits. Both the large and small kymographs are arranged so that the kymogram can be taken either with the grid or the film moving and are adapted for a filmkasette of 24×30 cm. On the kymograph with a moving film the continuity of the contour of the organ is obtained. If corresponding points on the kymogram are connected with one another the border of the organ appears unbroken (Fig. 2). On the other hand kymograms taken with a moving film show the contour of the organ in steplike stages. Corresponding points in this case lie at right angles to the slits (Fig. 3).

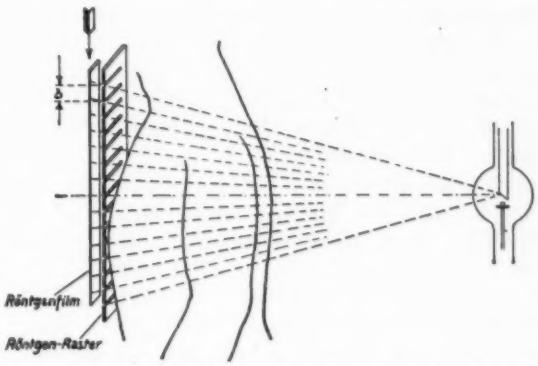

Fig. 1. Diagram of the mode of action of the STUMPF röntgenkymograph. (From STUMPF: Das Röntgenographische Bewegungsbild und seine Anwendung.)

With a moving grid one does not obtain a registration of the movements of one and the same point but rather of continually new points within a small section of the cardiac border. With moving film and stationary grid the same points in the cardiac contour always appear in the slits in one and the same phase of movement. The ideal would naturally be to be able to follow kymographically the movements of one and the same point during a complete cardiac cycle. Because of the threedimensional movements of the heart, this is not obtainable in registration with either moving film or moving grid. In both cases a registration of the movements of a small section of the cardiac contour is obtained, although in the former case this section is distinctly smaller than in the latter. In both cases however, the more marked the cranio-caudal movements of the heart are, the larger is the section registered. As STUMPF points out, it is to be assumed that in an organ as large as the heart, points of the cardiac contour situated close to one another are carrying out similar if not the very same movements. In such a gross registration as is obtained with the STUMPF kymograph, scarcely any rôle is played by this difference in accuracy between the two methods of procedure. If on the other hand one wants to obtain really detailed cardiac kymograms, registration with moving film and

stationary grid becomes an unavoidable necessity and in that case the STUMPF apparatus is no longer adequate. According to our experience in kymography ad modum STUMPF, it plays no essential rôle whether the registration is made with moving film or moving grid. Kymograms taken with a moving grid are often to be preferred because they are more comprehensible and surveyable, especially for the uninitiated. As a rule a supplementary kymogram with moving film seems not to have provided us with any more information.

With regard to the technique, the cardiac kymogram is taken usually as dorsoventral pictures with a sagittal direction of the rays, a tube focal distance of about 1 meter and the patient standing. In most places the velocity of the grid or of the kasette seems to be constantly set at 3 seconds. The construction is such that one can figure out the set-up for a desired velocity. Since the velocity should be adapted to the heart frequency, a considerable disadvantage of the STUMPF kymograph is the fact that there is no convenient way of knowing the actual speed when one uses the device for the alteration of the velocity. Special determination of this velocity is thus required. As far as the load is concerned, at St. Erik's Hospital where the small kymograph has been in use since June 1932, we have used 65—80 KV (effective tension) and 50 MA with a sagittal beam, this corresponding to STUMPF's instructions.

As a complement to the kymograph, STUMPF has constructed a kymoscope, by means of which one can visualize the movements registered on a kymogram. The kymoscope has thus the same function in kymography as a projector in cinematography.

As SCHILLING among others has pointed out, kymography is not intended to replace röntgen cinematography. It has, however, the advantage that it is not an expensive method of investigation, there is no danger of injury from radiation and it presents for analysis the separate phases of the heart action on one single film.

The normal cardiac kymogram shows along the left contour within the left ventricular curve, asymmetrical, tooth-like serrations each and every one of which represent a cardiac cycle (Fig. 4). The vertical distance between a line drawn through the tips of the serrations and one through their bases gives a measure of the kymographic beat amplitude. Serrations which lie the same distance from the starting position of the slits belong to the same cardiac cycle. On a usual cardiac radiogram the left auricular curve is only occasionally distinctly represented, and as a rule it is difficult to isolate. On a normal cardiac kymogram however there appear, almost without exception, quite small serrations which are double or notched in contrast to those within the left ventricular curve. (Fig. 5.) These are found between the pulmonary and the left ventricular contour within a small area whose extent varies from case to case.

These double serrations are believed to originate in the left auricle. In this connection it may be mentioned that ARENDT and BAUMANN pointed out that a more exact determination of the BORDET points and especially of the important point *G* is possible with kymography than with orthodiagraphy. *G* in the BORDET scheme for estimation of the size of the heart corresponds to the area of the left auricular pulsations on the kymogram. In the pulmonic area and the left aortic arch, simple serrations again appear although with a reversed form in comparison to the left ventricular serrations. Along the right vascular curve there are as a rule small, usually notched serrations which are interpreted as pulsations or variations in pressure within the superior vena cava. If the aortic arch is much widened, typical aortic pulsations with simple serrations are obtained on this side. The right auricular contour does not show the same uniformity with regard to pulsations as do the other sections of the cardiac silhouette. In its upper part there appear as a rule double or notched serrations of the same type as in the left auricular outline while its lower part shows simple serrations of the same appearance as in the left ventricular contour. (Fig. 6 a) and b).) The extent of the double or the simple serrations along the right auricular outline can be extremely variable and a possible finding of only double or only single serrations along the whole right contour signifies in itself nothing pathological.

A further inspection of the pulsations in the left ventricular outline shows that the serrations there can have a very variable appearance. Cardiac kymography is of course a two-dimensional registration of three-dimensional movements. Each serration thus represents the product of a number of different movements. The configuration of the serrations is changed according to whether one or another movement is dominating. On registration with horizontal slits the heart with insignificant cranio-caudal movements and large medio-lateral movements shows particularly pointed, horizontally drawn out serrations because the more the cranio-caudal movements make themselves felt, the rounder the serrations become. The relation between cardiac frequency and the velocity of the grid or of the kasette also plays a considerable rôle in the appearance of the serrations. This relation must always be the same if kymograms of the same heart made on different occasions are to be fully comparable. The greater the velocity in relation to cardiac frequency, the wider the serrations.

Altogether the most usual type of serrations along the left ventricular curve are lanciform or tooth-shaped (»einfache Hakenform») with one straight and one more or less curved edge. (Fig. 4.) STUMPF states that this type of serration was encountered along the left contour in 60 % of 250 cases of young healthy hearts. This lanciform peak is usually

most marked in the middle part of the ventricular outline while the serrations down toward the cardiac apex often take on a more rounded form. As STUMPF points out this probably depends on the fact that the craniocaudal movement of the cardiac apex has asserted itself. These serrations with rounded apices can sometimes appear along the entire left ventricular contour particularly in a number of cases of bradycardia. It cannot be correct, as STUMPF asserts, that these occur especially in myocarditis. At least no support is obtained for this conception in the large series of kymograms with autopsy controls from St. Erik's Hospital.

The site of the greatest pulsatory excursions has been discussed many times in röntgen literature. DIETLEN and many others consider that the greatest amplitude of the beat is found at the cardiac apex and that this gradually decreases toward the atrioventricular boundary. LAURELL expresses himself more cautiously and says that it seems as if the apex of the heart usually has the greatest beat in an erect position. In dorsal decubitus on the other hand he finds the greatest amplitude of the beat toward the middle of the left ventricle and only small or scarcely any pulsations at the apex. LAURELL attempts to explain these differences by the cephalic movement of the diaphragm in decubitus with a resulting greater fixation of the cardiac apex.

STUMPF bases his grouping of two types of pulsation in the left ventricular outline on the investigation of the 250 young, healthy hearts mentioned above. Type I is characterized by having the maximum beat amplitude at the cardiac apex. Type II shows the reverse and the greatest excursion of the pulsation is encountered at the base of the heart. In STUMPF's material, 20 % of the cases belonged to type II and these hearts were supposed to have shown signs of a smaller cardiac reserve with an earlier rise in blood pressure on exercise as well as a slower recovery afterwards. According to STUMPF one should usually find type II in marked valvular disease and other organic lesions of the heart. With due observance of STUMPF's instructions, I have classified 400 different cardiac kymograms from St. Erik's Hospital. As table I shows, more than half of the series (213) were cases of clinically positive valvular disease and myocarditis in compensating or decompensating stages and despite this, only 55 % belonged to type II. Out of the 79 clinically healthy hearts, almost half (49 %) showed pulsations of type II. Of the entire 400 hearts, 154 belonged to type I, 206 to type II and 40 were transition forms between type I and II. Thus this material offered no support for STUMPF's conception that type II is encountered oftener in valvular disease and myocarditis than in healthy hearts. At present it therefore seems to us as if this division into two types of pulsation has no clinical significance.

Table I

The material studied comprised 400 different cardiac kymograms, which may be classified as follows:

a)

Clinically normal hearts	79
Clinically indefinite cases where heart disease could not be positively excluded	66
Hearts with large pleuropulmonic processes	4
Hypertonic hearts without marked aortic changes or signs of myocardial injury in the form of decompensation	38
Hearts with valvular diseases and myocarditis	213
Total	400

b) Classification according to STUMPF's types of pulsation:

Type I	154 = 38.5 %
Type II	206 = 51.5 »
Transition forms	40 = 10 »
Total	400

c)

	Total	Type I		Type II		Transition types	
	No.	No.	%	No.	%	No.	%
Clinically normal hearts	79	30	38	39	49	10	13
Hypertonic hearts	38	17	45	19	50	2	5
Hearts with valvular disease and myocarditis	213	76	36	117	55	20	9

Normally a certain relation exists between the frequency and the amplitude of the heart beat. A low frequency is associated with a large amplitude and vice versa. The well known explanation is, that with a decreasing frequency, it is chiefly diastole which is prolonged. Such a decrease in frequency should give greater filling and a resulting increase in the amplitude of the beat. The conclusion that a similar relation must exist between the amplitude and volume of the beat has afterwards been drawn from the undoubted relation which normally exists between beat-amplitude and beat-frequency. In many hearts under certain conditions there is probably a relation between cardiac frequency and the amplitude of the beat on one side and the volume of the beat on the other but as LAURELL emphasizes this is far from constant. Thus for example the type of heart in aesthenic individuals often shows a large beat-amplitude with an increased cardiac frequency, despite the fact that according to the BJURE-LAURELL investigations the beat- and minute-volume are decreased. Thus stronger pulsations may sometimes be an expression of an increased just as well as of a decreased beat-volume (LAURELL). Now and then one encounters remarkably small pulsations along the left contour in hearts of practically normal size but it cannot be correct to draw from these any definite conclusions as to the size of the beat-volume. We do not know any absolute principle for the work of the cardiac mus-

culature. There is much in favour of LAURELL's theory that the essential factor consists in a movement of the base toward the apex so that the atrio-ventricular septum works like the piston of a pump and while it moves toward the apex, draws blood into the auricle. The absence of relationship between the beat-amplitude and the beat-volume can be explained to a certain degree in this way. In this connection it should be remembered that the decrease in volume which the heart undergoes during systole does not correspond to the mass of the blood which is forced out. At the same time as the chambers contract there is a suction and accumulation of blood in the auricles.

SUNDBERG has made comparative investigations of the first cardiac sound which usually occurs during the contraction period of the heart and the movements of the heart shadow and has come to the conclusion that the period of isometric contraction of the ventricle corresponds to the last part of the lateral movement of the cardiac contour. The cardiac kymographic curves recently published by ZDANSKY and ELLINGER are not in complete accord with these observations. There the isometric period is represented by a small plateau-like flattening of the curve or by such a minimal lateral displacement of the cardiac contour that it is impossible to observe on a fluoroscope. The ZDANSKY-ELLINGER experiments suffer however from a lack of reliability in the matter of distinction of the different phases of the cardiac cycle as electrocardiograms were not taken simultaneously. — The velocity commonly used with the STUMPF apparatus is too long to allow of a differentiation of the period of isometric contraction and emptying on kymograms taken with this instrument. It is true that in a recent article, supported by simultaneously taken sphygmograms and curves of the cardiac apex, STUMPF attempts to distinguish the isometric and emptying periods on the left ventricular serrations of his kymograms, taken with a 3 second revolution of grid and film kasette. These comparable curves are however so extra-ordinarily small that they are not convincing.

On the STUMPF kymogram small extra serrations appear now and then within the left ventricular contour, usually in the period immediately after the medial movement of the cardiac border (Fig. 7). In hypertension hearts with widened aorta, these are found almost constantly but they sometimes occur in hearts which are clinically completely healthy. It seems to us most probable that these extra serrations are due to an aortic recoil. Simultaneously taken kymograms and sphygmograms should be able to explain in such cases the possible relation between these extra serrations and the dicrotic wave.

In a number of cases where the electro-cardiogram showed a branch-block, the ventricular serrations showed a more or less marked notching at the apices. Fig. 8 is taken from a case where the electro-cardiogram

showed a complete block with an auricular rate of 78 and a ventricular rate of 33 beats per minute while the ventricular complex showed an incomplete left-sided branch-block. It does not seem very plausible that in such cases each serration should represent its own ventricular contraction, especially as we have observed a similar notching in cases where the electro-cardiogram showed only myocardial injury of an indefinite type.

It has been pointed out above that the STUMPF kymograph gives such a crowded curve of the movements of the left ventricular contour that a more thorough detailed study is almost completely impossible. The same is true with regard to the pulsations of the aortic and pulmonary arches. In this case the serrations give only a general and extremely summarized picture of the movements. By means of simultaneously taken sphygmograms from the left subclavian artery and the curves of the cardiac apex, STUMPF has proven that the lateral movements of the aorta on the kymogram correspond to the expulsion phase of the heart and that the small incisure which now and then appears on the sloping limb of the aortic serration corresponds to the closure of the aortic valves. STUMPF points out that larger pulmonary than aortic serrations are seen in disease of the mitral valve and this is in accordance with our experience. Normally the reverse of this situation is encountered. The character of the grid as a secondary diaphragm makes possible a very thorough exposure, resulting in a distinct picture of the aorta, particularly in cases with arteriosclerotic changes. It is especially interesting to determine how little obstruction extensive calcification makes in the pulsatory excursions of the aortic wall. The kymogram can often be of invaluable help in the diagnosis of aneurysm of both the ascending and descending aorta. If the aneurysm is not completely thrombosed it shows typical aortic pulsations (Fig. 9). The kymogram becomes decisive in the differential diagnosis between aneurysm and mediastinal tumors such as intrathoracic goitre.

The pulsations within the right auricular contour have always been a debatable subject in röntgen literature. Numerous authors have based their conceptions exclusively on observations of fluoroscopic pictures. A number of authors, VAQUEZ-BORDET among others, assert that normally they never see any auricular pulsations within the right auricular contour while others maintain the opposite. GROEDEL states that the auricular pulsations are very small and that they are presystolic in relation to the apex beat. Within the lower part of the right auricular contour in more active heart action, one often sees typical ventricular pulsations which GROEDEL explains as transmitted ventricular pulsations. DIETLEN has a similar conception and considers that the typical ventricular pulsations which can sometimes be observed far down are trans-

mitted. ARNSPERGER and several others also maintain that they have observed presystolic auricular contractions. Of especial interest in this connection are the results which GÖTT arrived at with his kymographic experiments in 1912, which were the first objective registration of pulsations. He obtained both ventricular systolic pulsations and double serrations along the right contour. No presystolic serrations appeared however and this led LAURELL to express the supposition that the general röntgenological conception of the observability of auricular systole was not completely correct.

The STUMPF kymograph has put new life into the discussion of the pulsations of the right border of the heart. Kymographic studies have made one doubt the description in anatomy texts and atlases of the right cardiac border as altogether formed by the right auricle — a somewhat startling result in the field of topographical anatomy. (See for instance CORNING's Lehrbuch der topographischen Anatomie). The theory that the typical ventricular pulsations appearing along the right contour are transmitted, as expressed by GROEDEL, DIETLEN and others, seems to STUMPF rather improbable. He suggests instead the possibility that the old conception, of the right auricular curve being formed by the right auricle only, may hold good for the heart in a lying position as it is based exclusively on post mortem observations. In an upright position the heart should be rotated according to STUMPF so that the right ventricle normally forms the border in the caudal part of the right auricular outline. In this way STUMPF explains the fact that 90 % of his cases showed pure ventricular pulsations in the caudal part of the right contour. STUMPF thus revives the SCHWARZ theory of 1911 regarding the type of heart found in aesthenic individuals. The ventricular systolic pulsations which are observed in such hearts along the greater part of the right auricular contour are not transmitted but are due to a rotation of the heart to the right so that the right ventricle forms the border.

Neither STUMPF himself nor others using this kymograph have been able to bring forward any definite proof of the correctness of his conception as to the topographical anatomy of the right auricular contour. As a rule it cannot be correct to draw conclusions as to the relation between the auricle and ventricle on the basis of the configuration of the serrations. The possibility that the thin-walled and weak-muscled right auricle could be highly influenced by the activity of the ventricles does not seem to have been sufficiently taken into consideration. However, one can sometimes obtain kymograms where the border between double and single serrations is so sharp that one is inclined to suppose that this marks the anatomical atrio-ventricular boundary. (See fig. 6 a.) Decisive proof as to the topographical anatomy of the right auricular contour will probably only be obtained from a careful examination of autopsy materia

where special attention is paid to eventual changes due to lying and upright positions.

STUMPF points out that one only exceptionally finds double serrations along the whole right auricular outline and these are usually pathological cases. As mentioned previously in over 90 % of his material, STUMPF found pure ventricular pulsations in the caudal part of the right contour. — In the material from St. Erik's Hospital, reported in this paper, 52 (13 %) out of 400 kymograms showed pure auricular pulsations or, more specifically expressed, double serrations along the whole right auricular outline. Table II shows the distribution of these 52 cases in the different cardiac groups. This summary thus gives on the whole exactly the same results as STUMPF obtained from his. In the greater number of the cases single serrations were encountered in a varying degree along the right contour of the heart. In at least 10 % of the cases however one sees small double serrations or so-called auricular pulsations. On the other hand there was no support for the STUMPF conception that this approximate 10 % would preferably be found in pathological cases.

Table II

Of 400 cardiac kymograms, 52 showed pure »auricular pulsations» along the entire right auricular contour. These may be classified as follows:

Clinically normal hearts	(79)	11 = 14 %
Clinically indefinite hearts	(66)	13 = 20 »
Hearts with large pleuropulmonic processes	(4)	1 = 25 »
Hypertonic hearts	(38)	5 = 13 »
Hearts with valvular disease and myocarditis	(213)	22 = 10 »

Now and then it may be difficult to decide what should or should not be considered auricular pulsations as ventricular serrations often show a more or less marked notching at the tips. In such cases we have interpreted the ventricular serrations as having been transmitted through an auricle which does not assert itself through independent serrations of its own although it actually forms the border (Fig. 6 b).

The respiratory phase in which the kymogram is taken is important in the appearance of the pulsations along the right contour. Only kymograms taken in the same respiratory phase of the same heart are absolutely comparable. Kymograms taken in expiratory and inspiratory phases often show obvious differences. It is usually possible to follow the double serrations considerably further down on the right contour in kymograms taken during inspiration than during expiration. This is probably related to the increased filling of the right half of the heart during inspiration.

A number of German authors (A. WILKE, H. CRAMER and H. H.

WEBER) believe that in cases where double serrations are observed along the whole right auricular contour, there is an overfilling of the right auricle (»latente Rückstauung») constituting the first sign of an overloaded heart. In addition to the double pulsations along the entire right auricular outline there was slight dyspnea on exertion and cardiac palpitation in the cases described by these authors. After a period of digitalis treatment those difficulties disappeared and single serrations appeared in the caudal part of the right contour.

With the purpose of finding out how the pulsations of the right auricular silhouette could vary in appearance under different conditions, we carried out control investigations in 12 cases after confinement in bed, digitalization and muscular work. The most suitable form of muscular exercise seemed to be to weight the arms with heavy dumb-bells, as experience has shown that patients with insufficient hearts as a rule have difficulty in carrying heavy loads. There was in addition the possibility of fluoroscopic control during the work-test and control kymograms could be taken at regular intervals without altering the patient's position. In cases where single serrations were found along the lower part of the right auricular contour at the first examination, no change in the pulsations was obtained during the work-test. Many hearts with double serrations along the whole auricular contour showed no change in pulsations after a period of confinement to bed or after confinement to bed + digitalization. Two hearts on the other hand gave positive results. In the caudal part of the right contour in both these cases, single ventricular serrations occurred after a period of lying in bed. After holding the dumb-bells, double serrations appeared along the entire right auricular outline. In both cases there existed a clinical suspicion of a heart affection as both complained of palpitation and dyspnea on slight exertion but otherwise there was nothing abnormal. The electrocardiogram showed nothing pathological in either case. Fig. 10 shows a section of the right contour from one of these two cases. On admission there were only double serrations along the right auricular border (a). After a period in bed, single serrations appeared in the caudal part of the outline (b). The two last sections are from the work-test. The former (c) comes from the control kymogram taken immediately before the test and the latter (d) is taken after holding the load for 5 minutes. This latter shows beautifully how the double serrations return along the entire auricular contour. It would be premature to draw any definite conclusions from these two cases. It is possible that these changes which we have been able to produce in the right auricular outline are an expression of a minor myocarditis. On another occasion I hope to be able to return to this point after we have obtained a larger series and have rationalized the work-test.

As to the origin of the double serrations, which STUMPF and many other authors in this field call auricular pulsations, it seems to have been agreed upon until now that one tip in the double serration represents the auricle's own pulsation and the other comes from transmission of ventricular movements. As a support for this conception, the only observation which could be made on the kymogram was the special significance attached to the fact that one of the two tips is often very indefinite along the most caudal part of the right contour, afterwards increasing in size until finally towards the base of the heart it becomes just as large as the other tip. The absence of comparable electrocardiographic and kymographic records is undoubtedly particularly important in the interpretation of the double serrations. The field has been open for all types of guessing and opinions seem to have been especially divergent with regard to the localization of auricular systole on the curve. STUMPF considers that when the latter of the two tips appears during ventricular diastole, the second medial movement in the double serrations should be that corresponding to auricular systole. According to him the other parts of the serrations are due to the auricle passively accompanying ventricular movements. Other authors (such as WILKE) believe that the first medial movements are due to auricular contraction and that the later tips are formed by the transmitted ventricular contraction. Neither of these two theories seems to be satisfactory. In one case the STUMPF conception may be correct while in another case the WILKE theory may hold good. Finally when one sees isolated cases of auricular fibrillation with double serrations along the right auricular contour, one has a tendency to suspect that auricular systole does not contribute at all to their formation.

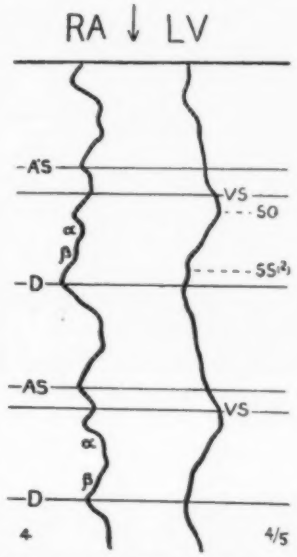

Fig. 11. (From ZDANSKY-ELLINGER: Röntgenkymographische Untersuchungen am Herzen.) Kymogram of the right and left cardiac border from a woman 28 years of age with a right-sided pneumothorax. A. S. = Auricular systole. V. S. = Ventricular systole.

From the investigations of ZDANSKY and ELLINGER, we have obtained a more detailed curve of the movements of the right auricular border. Their kymographic curves show as a rule two distinctly separated waves within the right auricular contour. They consider that one of these corresponds to the isometric period and that the other appears during

the last part of systole (Fig. 11). Making use of LAURELL's theory, these authors venture to explain the occurrence of a shallow trough between the waves as due to a sucking effect upon the auricular wall from the movement of the atrio-ventricular septum toward the apex during systole. Under favorable conditions they have also obtained a third presystolic tip which should correspond to auricular systole. As a rule, however, this third tip is not very prominent. It has already been pointed out that the ZDANSKY-ELLINGER investigations suffer from the lack of electrocardiographic control and therefore their curves cannot be considered as proofs. They do however support our conception that auricular contraction is normally altogether too small to appear on the STUMPF kymogram with the usual revolution time of 3 seconds. Nevertheless we have occasionally obtained triple tips instead of double along the right contour and it is possible that one tip in these cases is caused by auricular systole.

As has been mentioned in the foregoing, the kymogram often gives a valuable basis for diagnosis in cases of mitral insufficiency. Many mitral valvular lesions show larger pulmonary than aortic serrations. To trace with sufficient accuracy the posterior outline of a bulging auricle may sometimes be difficult. By filling the oesophagus with opaque material one usually obtains a definite outline but this is also possible with a kymogram taken with a moving grid in the first oblique projection. As one would expect, the kymogram of well marked aortic

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Plate I.

Fig. 2. Normal cardiac kymogram taken with a moving grid.
Fig. 3. Normal cardiac kymogram taken with a moving film.
Fig. 4. Pulsations of the left ventricle. Lanciform or toothshaped serrations. (»einfache Hakenform».)
Fig. 5. Double serrations along the left auricular contour.

Plate II.

Fig. 6. Different types of pulsations along the right auricular border.
a) Small double serrations in the upper part of the border.
b) Ventricular pulsations are coming through but the serrations are still notched at the tips.
Fig. 7. Small extra serrations along the left ventricular border in a hypertension heart with a widened aorta.
Fig. 8. A case of complete heart-block with incomplete left bundle branch-block.
Fig. 9. Aneurysm of the aortic arch.

Plate III.

Fig. 10. A case showing variations in the pulsations along the right auricular border under different conditions.
Fig. 12. Complete heart-block with a ventricular beat of 38 per minute.
Fig. 13. Pericarditis with effusion.
Fig. 14. Pleuropericardial adhesions along the left ventricular border.

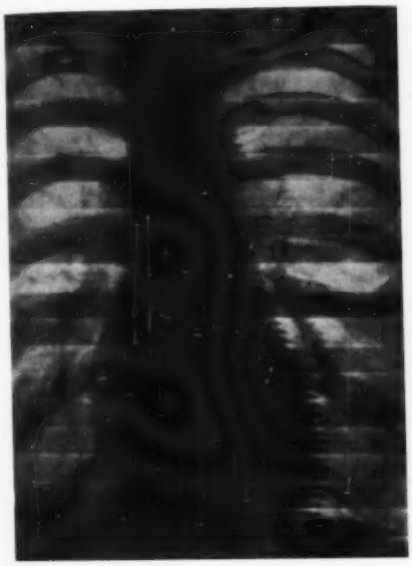

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6 a.

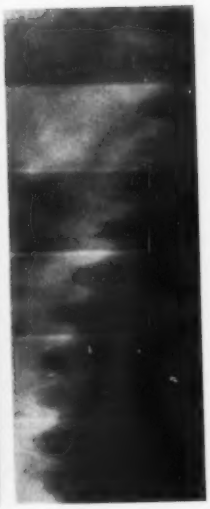

Fig. 6 b.

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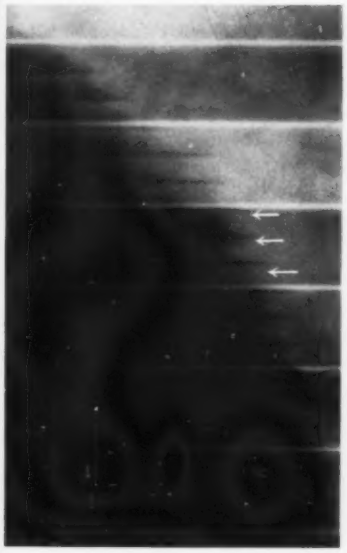

Fig. 7.

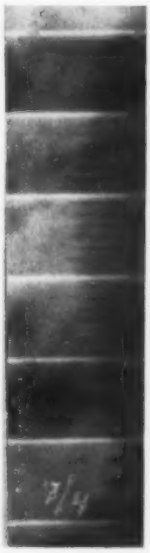

Fig. 10 a.

Fig. 10 b.

Fig. 10 c.

Fig. 10 d.

Fig. 8.

Fig. 9.

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Fig. 12.

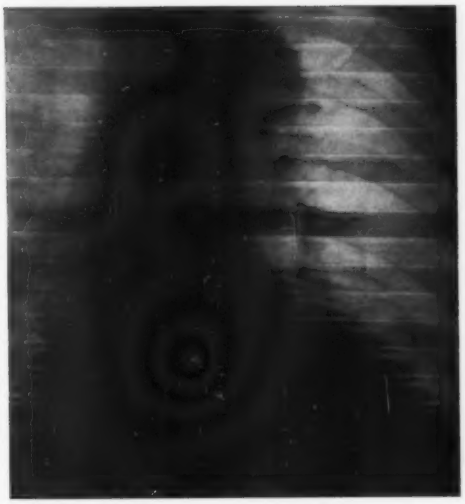

Fig. 13.

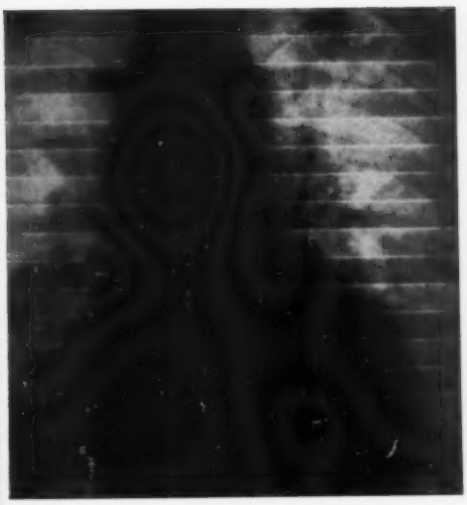

Fig. 14.

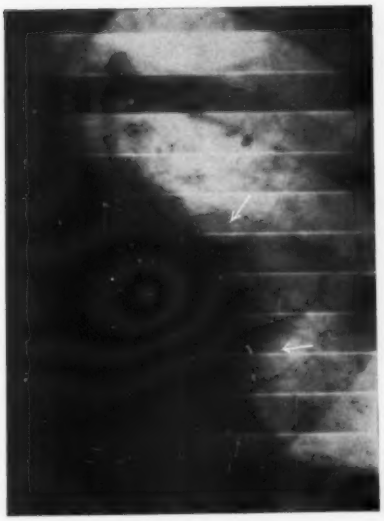

Fig. 15.

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valvular disease gives an extraordinarily characteristic picture. The rocking movement and the large pulsations of the fluoroscopic pictures are represented by long drawn out, pointed left ventricular serrations with a particularly large beat amplitude along the ventricle as well as along the aortic arch. As mentioned previously small extra tags are also almost constantly observed on the left ventricular serrations.

In slightly decompensated hearts the kymogram often gives valuable information. Visible pulsations are transmitted from the heart to the vessels and bronchi in the lung parenchyma to a greater extent than normally and this phenomena points to a passive pulmonary congestion. even if the usual radiogram gives no definite sign of it. In more well marked forms of pulmonary congestion one can observe how hilus lymphomas and the vascular trunks give such strong pulsations that the different types of serrations appear here also. In cases where venous congestion is especially marked, pulsations finally appear to an increasing extent in the superior vena cava.

Many disturbances in rhythm can be detected kymographically. There is, however, no chance of the kymograph reaching the accuracy and precision of the electrocardiograph, it can only give a coarser orientation of the types of irregularity. Single extra systoles and complete block usually offer no difficulty in kymographic diagnosis (Fig. 12). The possibility of kymographically diagnosing branch-block of different types has already been touched upon in another connection. As for auricular fibrillation, the most usual form of arhythmia next to extra systole, it can be easily recognized in many cases by the lack of similarity in adjacent serrations. As a rule only 3—5 cardiac cycles are registrated on the same kymogram; if all these serrations are rather regular in appearance one sometimes ventures to exclude an arhythmia even if the electrocardiogram shows a fibrillation.

The exudative pericardites give an extraordinarily characteristic picture in clear cut cases. The exudate preferably collects up over the base of the heart around the vascular trunks so that the normal cardiac contour is more or less completely obscured. As a result no real pulsations should be observable at the base of the heart in cases with a large accumulation of exudate. This is in agreement with the kymographic picture of an exudative pericarditis. Fig. 13 shows the kymogram from a patient with such a condition, where at autopsy 300 c. c. of pericardial fluid were found. At the cardiac apex the pulsations were distinct, while up towards the base of the heart they were almost completely obliterated by the exudate. In the lungs there were marked signs of stasis with increased pulsation of vessels and bronchi. It should be added here that it is not possible to diagnose pericardial synechiae from a kymo-

gram alone. On the other hand the kymograph is of great help in demonstrating pleuro-pericardial thickening (Fig. 14).

We used to take kymograms of all hearts sent for röntgenological cardiac examination but we now use the kardiograph for all cases where the size and the appearance of the pulsations can be expected to have differential diagnostic value. This is especially true in cases of suspected mediastinal tumor, aneurysm, and enlargement or change in the mediastinal shadow which may be related to the heart. In addition we use the kymograph to determine the type of pulsation in separate sections of the heart in different forms of valvular disease and myocarditis.

According to our experience the kymographic method of investigation has proven itself a valuable diagnostic aid in the röntgenological examination of the heart. It has aroused our interest and brought us into contact with problems with which we used to be unfamiliar. It has emphasized the difficulty of distinguishing physiological and pathological conditions.

In conclusion I wish to express my gratitude to my chief Dr CARL SANDSTRÖM for his kindness in placing the kymogram material of the hospital at my disposal.

SUMMARY

A report is given of the results obtained with the small STUMPF kymograph which has been in use for one year in St. Erik's Hospital. This method has shown itself to be an extraordinarily helpful addition to the usual röntgen examination of the heart, in that it makes possible a more refined diagnosis of cardiac conditions and a detailed study of the movements of the different parts of the organ. In the diagnosis of pleuro-pericardial lesions and pericarditis as well as in the differential diagnosis of aneurysm and mediastinal tumor, it has been of invaluable help and sometimes the only examination method by means of which one could make the correct diagnosis.

A study of the kymogram material from St. Erik's Hospital gave no support to the conception that the STUMPF division into two types of pulsation was of clinical significance. It was not possible to confirm STUMPF's assumption that double serrations along the whole right auricular outline are found especially in cases of heart disease. The author opposes the idea that any sure conclusions as to the topographical anatomy of the heart can be drawn from the configuration of the serrations. The pulsations along the right auricle have caused especial interest and special experiments have been carried out which prove that the double serrations can vary considerably in extent in each case under different conditions.

ZUSAMMENFASSUNG

Verf. berichtet über die Resultate, die mit dem seit einem Jahre am Krankenhause St. Erik in Gebrauch befindlichen kleinen STUMPFschen Kymographen erreicht wurden. Diese Methode hat sich als eine ausserordentlich wertvolle Bereicherung unserer Mittel bei der üblichen Röntgenuntersuchung des Herzens erwiesen, indem sie eine verfeinerte Diagnose kardialer Zustände und ein detailliertes Studium der Bewegungen der ver-

schiedenen Teile des Organs ermöglicht. Bei Diagnostizierung von pleurokardialen Läsionen und von Perikarditis wie auch bei der Differentialdiagnose zwischen Aneurysma und Mediastinaltumor war die Methode eine unschätzbare Hilfe, und mitunter war es das einzige Untersuchungsverfahren, durch welches eine korrekte Diagnose gestellt werden konnte.

Ein Studium des Kymogramm-Materials vom Krankenhause St. Erik gab keine Stütze für die Auffassung, dass die STUMPFsche Aufteilung in zwei Pulsationstypen von klinischer Bedeutung wäre. STUMPFs Annahme, dass Doppelpulsationen längs der ganzen Aussenkontur des rechten Vorhofes besonders in Fällen von Herzleiden gefunden würden, konnte nicht bestätigt werden. Verf. erhebt Einspruch gegen den Gedanken, dass aus der Konfiguration der Bewegungen sichere Schlüsse über die topographische Anatomie des Herzens gezogen werden können. Die Pulsationen längs dem rechten Vorhof haben spezielles Interesse erweckt, und es wurden besondere Versuche ausgeführt, die gezeigt haben dass die Ausdehnung der Doppelpulsationen im Einzelfalle unter verschiedenen Bedingungen beträchtlich variieren kann.

RÉSUMÉ

L'auteur communique les résultats obtenus avec le petit kymographe de STUMPF, qui est en service depuis un an à l'hôpital St-Erik. Cette méthode s'est montré un moyen auxiliaire très précieux dans l'examen radiologique habituel du cœur, en ce sens qu'elle permet un diagnostic plus précis des conditions cardiaques et une étude détaillée des mouvements des différentes parties de l'organe. Dans le diagnostic des lésions pleuro-péricardiques et des péricardites, comme aussi dans le diagnostic différentiel des anévrysmes et des tumeurs du médiastin, cette méthode a été d'un secours inappréciable et a parfois constitué le seul moyen de poser un diagnostic correct.

L'étude des kymogrammes pris à l'hôpital St-Erik ne confirme en aucune façon la conception d'après laquelle la division établie par STUMPF des pulsations en deux catégories aurait une valeur clinique. Il n'a pas été possible de confirmer l'hypothèse de STUMPF, suivant laquelle les movements double le long du contours de l'oreillette droite seraient un symptôme special de cardiopathie. L'auteur oppose cette idée qu'aucune conclusion certaine ne peut être tirée, au point de vue de l'anatomie topographique du cœur, de la configuration des serrations. Les pulsations le long de l'oreillette droite ont provoqué un vif intérêt et des expériences ont été faites, qui établissent que les doubles serrations peuvent varier notablement dans chaque cas, suivant les conditions.

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FROM THE RÖNTGEN DEPARTMENT OF THE ROYAL SERAPHIMER HOSPITAL, STOCKHOLM.
CHIEF PROF. GÖSTA FORSSELL

A METHOD FOR RÖNTGEN EXAMINATION OF THE HYPOPHARYNX AND UPPER AIR PASSAGES[1]

by

Gunnar Jönsson

(Tabulæ XX—XXI)

Inasmuch as the hypopharynx and the upper air passages are accessible to inspection, either directly or indirectly with the help of a mirror, röntgen examination of these regions usually seems to be considered of only secondary importance. COUTARD, however, points out the necessity of such an examination in all cases of malignant tumors of the larynx which are to be treated radiologically and BROWN, REINEKE and HAY as well as others have shown the value of this procedure in other pathological processes. In the first place, according to these authors a röntgenogram is sometimes indispensible in making the diagnosis. This statement holds good in cases where the changes are so localized that they are easily missed on clinical examination and also in cases where the examination is difficult to carry out, as for instance in hypopharyngeal tumors. In the second place, röntgen examination can not be dispensed with when it comes to determining the extent of the pathological process and its relation to neighboring tissues. In the case of tumors these characteristics must be studied if the eventual radiological therapy is to be effectively carried out. In addition, because it does not hurt the patient, röntgen examination is better than any other method of controlling the changes which develop during the course of treatment. These reasons are in themselves a sufficient motive for röntgen examination in cases of proven or suspected disease changes in the hypopharynx and upper air passages but the procedure is also valuable from other points of view. Experience has shown that cases are not infrequently sent for röntgen examination

[1] Read before the Swedish Society for Medical Radiology. Stockholm, Oct. 14, 1933. Submitted for publication Dec. 12th, 1933.

with an indefinite diagnosis and the roentgenologist, if his attention is called to this, can demonstrate a lesion of the upper air passages. It is of course obvious that the method is a valuable diagnostic aid in cases which are clinically difficult to examine (children, patients with lock-jaw etc.).

Usually the only technique recommended in röntgenological examination of the pharynx is the method based on the introduction of opaque material. In 1928 however, BROWN and REINEKE showed that the condition of these organs could be studied on a lateral film of the neck, taken with suitable technique, without the use of an opaque substance. Furthermore in 1913 and 1914, THOST and IGLAUER respectively had shown that pictures of the larynx could be obtained in this way. This is due to the fact that when the pharynx and larynx are filled with air they stand out against the surrounding soft tissues, which in their turn form a contrast to the bony structures of the cervical region. It is therefore possible to see deviations from the normal such as swelling of the soft parts and tumors bulging into the air passages. In this way many disease conditions can be discovered but it is of course much too one-sided to completely abstain from investigations with artificial opaque substances as some authors have done. The two methods should be used to complement one another. In examinations carried out exclusively with opaque material, smaller changes are often hidden and these appear distinctly on a usual lateral picture of the neck. On the other hand examinations with contrast material give valuable information which cannot be obtained with the other method.

By using both these methods the hypopharynx and upper air passages can be examined rather completely. As this region is for several reasons very difficult to examine and the interpretation of the findings is often not very definite, I have improved the examination method with a technical detail which supplements the part of the investigation carried out without the use of opaque material.

The procedure is as follows: The patient is told to pinch the nostrils together with one hand and then to expire with a closed mouth until he feels a tension in the ears (as in the Valsalva experiment). During this period a lateral picture is taken of the neck in the same way as the soft parts of this region are usually roentgen-photographed (film focal distance 2 meters, 70 kv, 150 ma, 0.3—0.4 seconds). According to KÖRNER, there may be the possibility of an atrophic ear drum bursting during Valsalva's experiment. The procedure should therefore be carried out with some cautiousness when the patient has previously had any middle ear disease.

By means of this technique the pressure in the upper air passages is raised, the walls are distended and the increased air content gives

a good contrast effect. Moreover, in normal cases the hypopharynx fills with air and it can be studied better than on a usual lateral film. If the hypopharynx does not widen, one should suspect that its walls are the seat of some type of infiltrative process which makes them stiff and unyielding. The soft palate is pressed forward and down and as a result the space in the nasopharynx becomes larger and it is easier to observe disease changes in that region. The walls of the larynx are stretched and the ventriculus Morgagni widens so that the true and false vocal cords are distinctly visible. Laryngeal details can also occasionally be seen on the usual lateral picture of the neck but this is not the rule. HAY considers that he succeeds in obtaining a satisfactory picture of the larynx in all women patients but in only 50 % of the men. By means of röntgen photography carried out during the Valsalva experiment, it is possible to get a clear picture of the details of the larynx in *every case*.

SUMMARY

The author describes a method for examination of the hypopharynx and upper air passages based on Valsalva's experiment.

ZUSAMMENFASSUNG

Verf. beschreibt eine auf Valsalvas Versuche gegründete Methode für die Untersuchung des Hypopharynx und der oberen Luftwege.

RÉSUMÉ

L'auteur décrit une méthode d'examen de l'hypopharynx et des voies aériennes supérieures, basées sur l'expérience de Valsalva.

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All pictures designated (a) were taken in the usual way; those designated (b) were taken while the Valsalva experiment was being carried out.

Plate I.

Fig. 1. Röntgenogram of a normal case. The air passage is widened in 1 b. The hypopharynx is air-filled so that the contours of the posterior and anterior walls show clearly as well as the wall between the larynx and hypopharynx. In normal cases the air forces its way down as far as the mouth of the esophagus at the level of the lower part of the cricoid cartilage but the orifice does not open. Underneath this there is often an air bubble in the upper portion of the esophagus. This probably consists either of air swallowed during the experiment or of air which had been lower in the esophagus and had risen with the increase in intrathoracic pressure. On the usual lateral view (1 a) of the larynx one cannot distinguish any details while in 1 b the vocal cords, the ventriculus Morgagni and the plica ventricularis are all distinctly visible.

Fig. 2. Röntgenogram of cancer of the hypopharynx. 2 a: The shadow of the prevertebral soft parts is wider than normal and the arytenoid region is considerably thickened. 2 b: When the patient raises the pressure in the upper air passages, the walls of the hypopharynx are seen to be absolutely stiff and immovable except high up where a slight widening of the lumen is obtained. There is considerable air in the upper part of the esophagus. The tumor involves all of the hypopharynx except the uppermost portion.

Plate II.

Fig. 3. Röntgenogram of a patient treated at the Radiumhemmet for cancer of the hypopharynx two years previously. She became symptom free after treatment except for relatively slight difficulty in swallowing which remained unchanged during the whole period and it was therefore concluded that the tumor was gone. In fig. 3 a the shadow of the prevertebral soft tissues is somewhat wider than normal and in fig. 3 b the walls, especially the anterior, are considerably thickened. They are however soft and movable and stretch out in a normal way.

Fig. 4. Röntgenogram of a tumor of the pharynx and nasopharynx. This shows much more distinctly on fig. 4 b than on 4 a.

Fig. 1 a.

Fig. 1 b.

Fig. 2 a.

Fig. 2 b.

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Fig. 3 a.

Fig. 3 b.

Fig. 4 a.

Fig. 4 b.

FROM THE PATHOLOGY DEPARTMENT OF THE RADIUMHEMMET, STOCKHOLM.
(CHIEF DR. REUTERWALL)

REACTIONS TO RADIATION IN LYMPH NODES CONTAINING CARCINOMA METASTASES OF THE SQUAMOUS CELL TYPE[1]

by

Leone McGregor, M. D., Ph. D.

(Tabulæ XXII—XXVIII)

Literature

In 1924 in a study of the effect of röntgen radiation on pathological tissues, PRYM came to the conclusion that all the changes produced by röntgen rays could also occur spontaneously and that one could not tell histologically whether a piece of tissue had been radiated or not. The differences between non-radiated and radiated tissues were at most only quantitative. All the changes seen following radiation could be explained by a primary effect on the tumor parenchyma and secondary changes in the vascular apparatus and connective tissue. In both cases there was vacuolar degeneration of the nuclei and cytoplasm of the cancer cells and the formation of foreign body giant cells. The destruction of lymphocytes immediately after radiation could also occur spontaneously near non-radiated necrotic cancer.

In his Caldwell lecture of 1925 EWING discussed tissue reactions to radiation. He felt that a large part of the destructive effect of rays upon tumors was caused by interference with the blood supply with resulting necrosis of the cancer cells and fibrosis of the capsule. When the tumor cells had invaded the lymph node capsule no radiation could control them. The plasma cell reaction was characteristic of radiation repair. Unless the plasma cell were derived from the endothelial leucocyte the latter cell was not important in the healing process although in the late stages it formed giant cells and foreign body tubercles which might resemble tuberculosis. After heavy röntgen doses he saw very cellular connective tissue develop in radiated nodes.

[1] Submitted for publication Jan. 10th, 1934.

Normal lymph nodes were comparatively resistant to radiation. He observed the following changes in a series of lymph nodes which had been heavily radiated: 1) the transformation of the germ center into a small compact ring of flat cells resembling squamous epithelium, 2) replacement of the germ center by lymphocytes, 3) obliteration of follicles but persistence of lymphocytes and 4) reticulum cell hyperplasia. Recovery took place after 3 or 4 months.

The necrosis, calcification and cysts seen in non-radiated cancerous nodes were ascribed to the effect of pressure from the capsule on the rapidly growing tissue. His material indicated a preponderance of connective tissue injury and reaction from röntgen rays and more tumor cell injury from radium.

He concluded that these tissue reactions were specific in the sense that taken as a whole they were not observed under any other conditions.

In 1925 QUICK and CUTLER described the radiation reaction in 40 specimens of metastatic squamous cell carcinoma in cervical lymph nodes. The non-cancerous nodes enlarged and showed hyperplasia with large prominent edematous follicles containing many mitoses and sometimes miliary hemorrhages. The carcinomatous nodes showed massive central necrosis which was in direct proportion to the amount of radiation. The effect was undoubtedly of vascular origin and must be regarded as anemic necrosis. A favorable radiation effect — marked regression of the tumor — was accompanied by a favorable reaction of the tissues adjacent to the tumor. This consisted of an active proliferation of the connective tissue, proliferation of young fibroblasts, exudation of lymphocytes, leucocytes and plasma cells, upgrowth of new capillaries and formation of granulation tissue. The tumor mass was broken up by invading connective tissue and the individual tumor cells underwent degenerative changes consisting of swelling of the cytoplasm, hydropic degeneration of the cell bodies, hornification, calcification, cell atrophy and complete necrosis. In several specimens no gross or microscopic evidence of tumor tissue could be demonstrated. The marked destructive effects were obtained by means of intensive irradiation with combined high voltage röntgen rays and radium. Small doses of radium alone or in combination with radium were wholly inadequate in their effects upon this resistant type of tumor cell. Then the center of the node showed the most marked changes, hornification, calcification and central necrosis, the adjacent tissues being only slightly altered.

In 1932 ENGLMANN described the effect of radiation on lymph node metastases of squamous cell carcinoma. There were large areas of necrosis and degenerative keratinization of the tumor cells. Nearby there were smaller nests of degeneration containing many giant cells. Although these giant cells were similar in appearance to Langhans or foreign body

giant cells, none of the cases had a tuberculosis infection and the giant cells were usually not lying beside degenerating cornified masses. Neither had there been any spontaneous tumor giant cells in the biopsy material removed prior to radiation. He therefore was convinced that these were derived from the cancer cells and were tumor giant cells. He considered that they could give rise to recurrences.

This brief review of the literature in this field shows that the problems are as follows:

I. Does radiation produce changes in cancer tissue which do not occur spontaneously?

II. Is the effect of radiation primarily on the cancer cells or does it first produce vascular changes which in their turn cause degeneration of the carcinomatous tissue?

III. What is the origin of the giant cells seen around these areas of necrotic carcinoma?

IV. What effect has radiation on lymphatic tissue?

V. Is there a histological difference in the effect of radium and röntgen treatment?

Material

During the years 1928 to 1932 inclusive, lymph nodes were removed following radiation in 41 cases of metastasis of squamous cell carcinoma. In 25 of these the nodes were cervical and in 16 inguinal. The primary tumors were situated as follows: lip 16, tongue 6, bucca 3, vulva 11, penis 2 and anus 3. There were available as controls 18 non-radiated cervical and inguinal lymph nodes containing squamous cell carcinoma metastases and 9 radiated non-carcinomatous cervical and inguinal nodes from cases of squamous cell carcinoma.

Methods

The diameter of these lymph nodes at the time of removal varied from 5 to 200 mm., the majority being between 70 and 150 mm. On account of the convenient size, sections could always be cut through the entire node. Numerous but not serial sections were made of each node. These were stained with hematoxylin-eosin, van Gieson, Weigerts elastic tissue stain and Bielschowsky silver stain. Frozen sections were stained for fat.

Radiation

The principles of the treatment of lymph node metastases used at the Radiumhemmet have been worked out by BERVEN and are described

by him in his publications on malignant tumors of the oral cavity. In accordance with these principles the lymph nodes are always first treated by external radiation with high voltage röntgen or preferably teleradium. When the nodes do not disappear and if they are freely movable they are then surgically extirpated. Moderate doses are given in these cases so that postoperative healing will not be disturbed. The time interval between preoperative radiation and removal is generally from 3 to 6 weeks. Usually during this period the skin reaction from the radiation disappears.

The teleradium treatment is given with LYSHOLM's or with SIEVERT's 3 gram apparatus. The former can be used at a 3 or 5 cm. skin distance while the latter is used at a 6 cm. skin distance. The running conditions in the röntgen treatment are as follows; about 170 kv. 6 milliamps. and 30, 40 or 50 cm. skin focal distances. 40 cm. is the usual distance and the THORÆUS »tin filter» was used in most of the recent cases.

The fractional method is applied in both teleradium and röntgen treatments. Only one of the necessary fields is treated each day and the daily dose is usually $^1/_4$ or $^1/_3$ HED. The total dosage varies with the local and general conditions in each individual case.

The following table gives the essential points in the treatment and pathological findings in the 41 cases. The nodes were removed from 1 day to $2^1/_2$ years after the last treatment. Five cases received röntgen only, 22 cases radium only and the remaining 14 both röntgen and radium treatment.

Microscopic Examination

The changes observed in the nodes will be discussed under the following headings: 1) the cancer cells 2) the reticulo-endothelium and lymphocytes 3) the tumor giant cells and giant cells of the foreign body type 4) the blood vessels and 5) the capsule.

1) *The cancer cells.* The very early effects of radiation on metastatic cancer cells cannot be discussed in this paper because none of the nodes were removed in less than 2 weeks after the first treatment.

The nodes which were extirpated 16 days, 3 weeks and 1 month respectively after the first radiation (cases 10, 6 and 12) all showed a more or less typical picture. Cornification and subsequent necrosis of all the cancer cells had apparently taken place (Fig. 1, 3 and 5). The picture in all 3 cases was that of larger and smaller masses of necrotic whorls of cornified epithelium, surrounded by a wall of reticulo-endothelium and giant cells of the foreign body type which were attached to one another and to the adjacent lymph node parenchyma through their processes. The reticulo-endothelial cells were proliferating and penetrating the border of the necrotic area.

Many of these cells were rounding off to form free mononuclear phagocytes. These were fusing to form countless numbers of giant cells which surrounded the entire cancer region. These giant cells with the help of the active reticulo-endothelium and mononuclear phagocytes were all attacking the cancer debris. In 10 and 12 the original structure of the necrotic mass could barely be detected. The nuclei were either completely disintegrated or visible only as shadow remnants. As far as could be determined from multiple sections through different parts of the entire node, the destruction of the cancer cells seemed to be complete. In places where the group of malignant cells had been very small the picture was often that of a foreign body epithelioid cell tubercle (Fig. 6). The cancer remnants, which were to be seen as small hyaline clumps or small masses of granular necrotic material, were surrounded by the hypertrophied reticulo-endothelial cells of the node in a more or less spherical arrangement interspersed with giant cells of the foreign body type, some eosinophils and a few plasma cells. These nodes all showed one or two large areas of necrosis as much as 1 cm. in diameter and external to these but internal to the capsule, numerous foreign body tubercles. One node (19) removed 17 days after the first radiation showed a different picture. There was very little necrosis and although most of the cancer cells were swollen and were undergoing all types of cytoplasmic and nuclear degeneration, there were still a good many mitoses.

The picture was not as uniform in *the nodes which were extirpated from 4 to 8 weeks after the first radiation.* Five of these (8, 9, 17, 24 and 32) showed exactly the same changes as the three nodes described above. There seemed to be complete necrosis of the cancer, which was surrounded by a wall of giant cells and mononuclear phagocytes. Nodes from 20 and 41 were very similar to these 5 cases except that, instead of the large necrotic cyst being entirely lined by giant or connective tissue cells, a portion of the cyst wall was formed by squamous cancer epithelium. In some places this wall had just as quiescent an appearance as normal squamous epithelium but in other areas strands and cords of cells were growing out from it externally to invade the remaining lymph node tissue. These cells were actively proliferating and there was no phagocytic or giant cell reaction in such areas. The center of the cancer necrosis seemed to be liquefied and contained many cholesterol crystals and polymorphonuclear leucocytes. The other nodes (21, 28 and 30) removed during the second month presented varying pictures. In 30 there was no massive necrosis but all the cancer cells showed marked signs of injury. It was impossible to tell whether they were capable of further growth. In 21 there was no necrosis, very little cellular injury and the cancer seemed to be growing slowly. In 28 there were large areas of necrosis but these were always lined by cancer epithelium which contained many

mitoses and was definitely invasive. In the two latter cases there was no giant cell reaction.

Many nodes were removed 3 and 4 months after the first radiation but some of these had been treated again shortly before operation. Two of the latter (3 and 14) showed complete necrosis of the cancer with the formation of a wall of giant cells, mononuclear phagocytes and reticulo-endothelial cells, in other words the same picture described above for 10, 6 and 12 removed 16 days, 3 weeks and 1 month respectively, after the first treatment. Most of the other nodes such as 18, 29, 33, 35, 37 and 39 extirpated 3 and 4 months after the first radiation contained large areas of necrotic hyperkeratotic epithelium surrounded by a wall of cancer epithelium with prolongations out into the node, which in 18, 37 and 39 contained mitoses. 31 was different in that a large cyst 1 cm. in diameter was lined by stratified squamous epithelium and contained only fluid and a few necrotic leucocytes. There were no remnants of cornified epithelium in the cystic cavity although there was cornification in other places in the node.

With one exception *the nodes removed from 5 months to 2½ years after the first radiation* all showed large areas of cancer necrosis surrounded by a wall of cancer epithelium from which cancer prolongations were growing out into the node. There was a giant cell reaction only around the smaller masses of completely necrotic cancer cells. Node 22 was the interesting exception (Fig. 2). It was removed 5 months after the first and 3 months after the last treatment and happened to have received the largest amount of radiation in the series. The cancer in this node, which is 1 cm. in diameter, seemed to be completely replaced by connective tissue. The capsule was very thick and very little lymphatic tissue remained. The whole center of the node was occupied by connective tissue in which there was a fluid filled cavity without any epithelial or endothelial lining.

When *the control series of 18 non-radiated squamous carcinoma metastases* were carefully scrutinized it was found that they also contained, (1) large areas of completely necrotic cornified cancer tissue surrounded only by a wall of giant cells of the foreign body type, mononuclear phagocytes and reticulo-endothelium (Fig. 4), (2) large and small areas of necrotic cornified cancer cells surrounded by a wall of squamous cancer epithelium, (3) large and small cysts filled with fluid and a few leucocytes and surrounded by a wall of squamous cancer epithelium, (4) small areas of necrotic cornified cancer surrounded by epithelioid cells and few giant cells and, (5) no areas of necrosis but marked signs of degeneration of large numbers of cancer cells with swelling and vacuole formation in cytoplasm and nuclei. In short, as far as the cancer cells themselves were concerned, practically every picture that was seen in the radiated nodes

could also be found in some of the non-radiated nodes. The only differences which could be observed were that there were usually more mitoses in the non-radiated nodes and that none of the latter showed complete necrosis of *all* the cancer masses.

2) *The reticulo-endothelium, reticulum and lymphocytes.* There was nothing different about the parenchymal reticulo-endothelium in the radiated cancerous, radiated non-cancerous and non-radiated cancerous nodes. In each group some nodes showed large, apparently active, reticulo-endothelium while in others the cells were almost difficult to find. On the other hand wherever the reticulo-endothelium came in contact with necrotic cancer cells, whether in radiated or non-radiated nodes, the same picture was seen. The reticular cells multiplied and hypertrophied and produced more reticulo-endothelial cells, mononuclear phagocytes and giant cells, all of which walled off the cancer. On one side the giant cells and mononuclear phagocytes attacked the cancer material while on their outer side they were attached by numerous processes to adjacent reticulo-endothelial cells (Fig. 7). In such a wall and in the tubercle-like areas around fragments of cancer necrosis, fine reticulum fibrils formed a complete meshwork between the hypertrophied reticulo-endothelial cells, the mononuclear phagocytes and the giant cells.

The lymphatic picture in these radiated lymph nodes was just as variable as in the non-radiated controls and could therefore be attributed to the different phases of the normal cycle in a lymph node. There were nodes without germinal centers, nodes with germinal centers packed with small lymphocytes, nodes with the reticulo-endothelial cells of the germinal centers swollen and filled with debris and nodes with these same cells arranged in whorls so that they resembled epithelioid tubercles. All transitions between lymphocytes and plasma cells were seen. There were often but not always more plasma cells in the cancerous radiated nodes than in the cancerous non-radiated nodes.

3) *Tumor giant cells and giant cells of the foreign body type.* Mononuclear tumor giant cells were present in many of the radiated and non-radiated lymphnodes. *Tumor giant cells* with two or more large irregular hyperchromatic nuclei were found in moderate numbers in 14 of the 41 radiated nodes and in 5 of the non-radiated (Fig. 9). Occasional mitoses were seen in these cells and the nuclei with their large nucleoli were very similar to those of adjacent cancer cells.

Multinucleated giant cells of the *foreign body type* occurred in enormous numbers in many of the radiated and non-radiated nodes. These giant cells contained small or large numbers of rather uniformly distributed nuclei of equal size, shape and chromatic content (Fig. 7). The nuclei were usually smaller and less chromatic than those of neighboring

Summary of 41 Cases of Irradiated Lymph

Case No. Biopsy No. Location Age Sex	Treatment								Time between first radiation and resection	Time between last radiation and resection
	Year	Date	Röntgen	Telera-dium	No. of fields	Distance	Filter	Date of operation		
			HED	total mg hrs		cm.	mm.			
1. 207/28 Pr. Ca. of Lip 77 years ♀	1928	25/1 29/1—27/1 5/2— 8/2 6/2	1/2	 11,000 20,000 7,800	 1 1 1	40 5 5 5	0.5 Cu + 1 Al 4 Pb. 4 Pb. 4 Pb.	13/3 1928	4 m.	6 d.
2. 572/29 Pr. Ca. of Lip 53 years ♂	1929	31/7— 1/8 8/10–11/10	2 × 1/2	12,000	2	40 5	0.5 Cu + 1 Al 4 Pb.	14/10 1929	2 1/2 m.	4 d.
3. 501/30 Pr. Ca. of Lip 46 years ♂	1930	28/2 5/3—11/3 6/5— 9/5	—	7,000 9,000 12,000	1 1 1	5 6 6	4 Pb. 6 Pb. 6 Pb.	20/6 1930	4 m.	6 w.
4. 833/30 Pr. Ca. of Lip 60 years ♂	1929 1930	30/4— 3/5 13/8—16/8	3 × 1/2	23,000	1	40 6	0.5 Cu + 1 Al	24/6 1930	19 m.	6 w.
5. 985/30 Pr. Ca. of Lip 63 years ♂	1930	1/4— 2/4 27/5—31/5	2 × 1/2	20,000	1	40 6	0.5 Cu + 1 Al 6 Pb.	7/11 1930	7 m.	5 m.
6. 130/31 Pr. Ca. of Lip 41 years ♂	1931	23/1—26/1	—	24,000	2	6	6 Pb.	15/2 1931	3 w.	2 w.
7. 586/31 Pr. Ca. of Lip 65 years ♂	1930 1931 10/4—13/4	8/8—10/8 1/1—10/1	2 × 1/2 9 × 1/6	 15,000	 3	40 40 5	0.5 Cu + 1 Al 0.44 Sn + 0.25 Cu + 1 Al 4 Pb.	24/6 1931	15 m.	2 m.
8. 756/31 Pr. Ca. of Lip 72 years ♂	1931	8/7—13/7 15/7—17/7	—	20,000 6,800	2 1	5 3	4 Pb. 4 Pb.	28/8 1931	7 w.	6 w.
9. 977/31 Pr. Ca. of Lip 62 years ♂	1931	29/8—29/8	—	5,000	1	5	4 Pb.	1/10 1931	6 w.	1 m.

Node Metastases of Squamous Cell Cancer

Microscopic findings in the lymph nodes
Old areas of necrotic cornified cancer undergoing organization, other areas of cancer with mitoses, few giant cells of foreign body type, plasma cells + +, old blood vessel changes +, thickened capsule.
Areas of cancer containing large fluid-filled cysts, a few mitoses, plasma cells + + +, much connective tissue formation, degenerative and proliferative blood vessel changes, capsule very much thickened (Fig. 15).
In one node, apparently complete necrosis of all cancer cells with formation of cysts filled with cornified debris and lined by giant cells of the foreign body type and reticulo-endothelial cells; plasma cells + +, some tubercle-like areas, many cholesterin crystals, blood vessel changes very slight, capsule thickened. In another node, necrosis of cancer cells with formation of cysts lined by cancer epithelium and filled with cornified debris; strands of cancer cells out in the node, plasma cells + +, many tubercle-like areas with many giant cells of the foreign body type, degenerative blood vessel changes slight, capsule much thickened and invaded by cancer cells.
Much connective tissue formation around very small groups of degenerating cancer cells, many tubercle-like structures, cholesterin crystals, plasma cells +, degenerative blood vessel changes + + +.
Necrosis of a large area of cancer cells with formation of a cyst partially filled with granular cornified debris and lined by cancer epithelium; strands of cancer cells with mitoses in the tips are invading the lymph node tissue, plasma cells +, eosinophils + +, much connective tissue, degenerative blood vessel changes + + + (Fig. 13).
Apparently complete necrosis of all cancer cells with formation of cysts filled with cornified debris and lined by giant cells of foreign body type and reticulo-endothelial cells; plasma cells +, some connective tissue formation, many tubercle-like areas, no blood vessel changes, capsule thickened (Fig. 5).
Much connective tissue formation around very small groups of degenerating or necrotic and cornified cancer cells, many mitoses in other cancer cells, many giant cells of foreign body type, plasma cells + + +, many neutrophils, many tubercle-like areas, degenerative and proliferative blood vessel changes, thickened capsule, necrosis of cancer nodule within the capsule (Fig. 10, 11).
Apparently complete necrosis of all cancer cells with formation of a cyst filled with cornified debris and lined by giant cells of foreign body type and reticulo-endothelial cells; plasma cells + +, degenerative blood vessel changes + (Fig. 7).
Apparently complete necrosis of all cancer cells with formation of a cyst filled with cornified debris and lined by giant cells of foreign body type, large fatty mononuclear phagocytes and reticulo-endothelial cells; some blood pigment scattered through the lymphatic tissue, no blood vessel changes.

Summary of 41 Cases of Irradiated Lymph

Case No. Biopsy No. Location Age Sex	Treatment								Time between first radiation and resection	Time between last radiation and resection
	Year	Date	Röntgen	Teleradium	No. of fields	Distance	Filter	Date of operation		
			HED	total mg hrs		cm.	mm.			
1. 207/28 Pr. Ca. of Lip 77 years ♀	1928	$^{25}/_{1}$ $^{23}/_{1}$—$^{27}/_{1}$ $^{5}/_{3}$— $^{9}/_{3}$ $^{6}/_{5}$	$^{1}/_{2}$	11,000 20,000 7,800	1 1 1	40 5 5 5	0.5 Cu + 1 Al 4 Pb. 4 Pb. 4 Pb.	$^{12}/_{5}$ 1928	4 m.	6 d.
2. 572/29 Pr. Ca. of Lip 53 years ♂	1929	$^{21}/_{7}$— $^{1}/_{8}$ $^{9}/_{10}$–$^{11}/_{10}$	2 × $^{1}/_{2}$	12,000	2	40 5	0.5 Cu + 1 Al 4 Pb.	$^{14}/_{10}$ 1929	2½ m.	4 d.
3. 501/30 Pr. Ca. of Lip 46 years ♂	1930	$^{28}/_{3}$ $^{5}/_{3}$—$^{11}/_{3}$ $^{3}/_{5}$— $^{8}/_{5}$	—	7,000 9,000 12,000	1 1 1	5 6 6	4 Pb. 6 Pb. 6 Pb.	$^{20}/_{6}$ 1930	4 m.	6 w.
4. 833/30 Pr. Ca. of Lip 60 years ♂	1929 1930	$^{30}/_{4}$— $^{3}/_{5}$ $^{13}/_{8}$—$^{16}/_{8}$	3 × $^{1}/_{2}$	23,000	1	40 6	0.5 Cu + 1 Al	$^{24}/_{9}$ 1930	19 m.	6 w.
5. 985/30 Pr. Ca. of Lip 63 years ♂	1930	$^{1}/_{4}$— $^{3}/_{4}$ $^{27}/_{5}$—$^{31}/_{5}$	2 × $^{1}/_{2}$	20,000	1	40 6	0.5 Cu + 1 Al 6 Pb.	$^{7}/_{11}$ 1930	7 m.	5 m.
6. 130/31 Pr. Ca. of Lip 41 years ♂	1931	$^{23}/_{1}$—$^{30}/_{1}$	—	24,000	2	6	6 Pb.	$^{13}/_{2}$ 1931	3 w.	2 w.
7. 586/31 Pr. Ca. of Lip 65 years ♂	1930 1931 	$^{9}/_{3}$—$^{10}/_{3}$ $^{1}/_{1}$—$^{10}/_{1}$ $^{10}/_{4}$—$^{15}/_{4}$	2 × $^{1}/_{2}$ 9 × $^{1}/_{8}$ 	 15,000	 3	40 40 5	0.5 Cu + 1 Al 0.44 Sn + 0.25 Cu + 1 Al 4 Pb.	$^{24}/_{6}$ 1931	15 m.	2 m.
8. 756/31 Pr. Ca. of Lip 72 years ♂	1931	$^{8}/_{7}$—$^{18}/_{7}$ $^{15}/_{7}$—$^{17}/_{7}$	—	20,000 6,800	2 1	5 3	4 Pb. 4 Pb.	$^{18}/_{8}$ 1931	7 w.	6 w.
9. 977/31 Pr. Ca. of Lip 62 years ♂	1931	$^{26}/_{8}$—$^{29}/_{8}$	—	5,000	1	5	4 Pb.	$^{1}/_{10}$ 1931	6 w.	1 m.

Node Metastases of Squamous Cell Cancer

Microscopic findings in the lymph nodes
Old areas of necrotic cornified cancer undergoing organization, other areas of cancer with mitoses, few giant cells of foreign body type, plasma cells + +, old blood vessel changes +, thickened capsule.
Areas of cancer containing large fluid-filled cysts, a few mitoses, plasma cells + + +, much connective tissue formation, degenerative and proliferative blood vessel changes, capsule very much thickened (Fig. 15).
In one node, apparently complete necrosis of all cancer cells with formation of cysts filled with cornified debris and lined by giant cells of the foreign body type and reticulo-endothelial cells; plasma cells + +, some tubercle-like areas, many cholesterin crystals, blood vessel changes very slight, capsule thickened. In another node, necrosis of cancer cells with formation of cysts lined by cancer epithelium and filled with cornified debris; strands of cancer cells out in the node, plasma cells + +, many tubercle-like areas with many giant cells of the foreign body type, degenerative blood vessel changes slight, capsule much thickened and invaded by cancer cells.
Much connective tissue formation around very small groups of degenerating cancer cells, many tubercle-like structures, cholesterin crystals, plasma cells +, degenerative blood vessel changes + + +.
Necrosis of a large area of cancer cells with formation of a cyst partially filled with granular cornified debris and lined by cancer epithelium; strands of cancer cells with mitoses in the tips are invading the lymph node tissue, plasma cells +, eosinophils + +, much connective tissue, degenerative blood vessel changes + + + (Fig. 13).
Apparently complete necrosis of all cancer cells with formation of cysts filled with cornified debris and lined by giant cells of foreign body type and reticulo-endothelial cells; plasma cells +, some connective tissue formation, many tubercle-like areas, no blood vessel changes, capsule thickened (Fig. 5).
Much connective tissue formation around very small groups of degenerating or necrotic and cornified cancer cells, many mitoses in other cancer cells, many giant cells of foreign body type, plasma cells + + +, many neutrophils, many tubercle-like areas, degenerative and proliferative blood vessel changes, thickened capsule, necrosis of cancer nodule within the capsule (Fig. 10, 11).
Apparently complete necrosis of all cancer cells with formation of a cyst filled with cornified debris and lined by giant cells of foreign body type and reticulo-endothelial cells; plasma cells + +, degenerative blood vessel changes + (Fig. 7).
Apparently complete necrosis of all cancer cells with formation of a cyst filled with cornified debris and lined by giant cells of foreign body type, large fatty mononuclear phagocytes and reticulo-endothelial cells; some blood pigment scattered through the lymphatic tissue, no blood vessel changes.

Case No. Biopsy No. Location Age Sex	Treatment								Time between first radiation and resection	Time between last radiation and resection
	Year	Date	Röntgen	Teleradium	No. of fields	Distance	Filter	Date of operation		
			HED	total mg hrs		cm.	mm.			
10. 1079/31 Pr. Ca. of Lip 70 years ♂	1931	$^{20}/_{11}$ $^{21}/_{11}$–$^{29}/_{11}$	$4 \times {}^{1}/_{3}$	3,500	1	5 40	4 Pb. 0.5 Cu + 1 Al	$^{6}/_{12}$ 1931	16 d.	11 d.
11. 307/32 Pr. Ca. of Lip 69 years ♂	1931	$^{4}/_{12}$ $^{5}/_{12}$– $^{7}/_{12}$	$^{1}/_{3}$ $2 \times {}^{1}/_{3}$	—	—	40 40	0.5 Cu + 1 Al 0.44 Sn + 0.25 Cu + 1 Al	$^{30}/_{3}$ 1932	5 m.	$2^{1}/_{2}$ m.
	1932	$^{14}/_{1}$—$^{15}/_{1}$	$2 \times {}^{1}/_{2}$			40	0.5 Cu + 1 Al			
12. 366/32 Pr. Ca. of Lip 48 years ♂	1932	$^{9}/_{2}$—$^{12}/_{2}$	$4 \times {}^{1}/_{3}$	—	—	40	0.5 Cu + 1 Al	$^{7}/_{4}$ 1932	1 m.	1 m.
13. 422/32 Pr. Ca. of Lip 65 years ♂	1931	$^{20}/_{7}$—$^{21}/_{7}$ $^{14}/_{9}$—$^{15}/_{9}$ $^{30}/_{1}$— $^{5}/_{2}$	$2 \times {}^{1}/_{2}$ $2 \times {}^{1}/_{2}$ $4 \times {}^{1}/_{3}$	—	—	40 40 40	0.5 Cu + 1 Al 0.5 Cu + 1 Al 0.5 Cu + 1 Al	$^{11}/_{2}$ 1932	8 m.	8 d.
14. 514/32 Pr. Ca. of Lip 35 years ♂	1932	$^{22}/_{2}$—$^{27}/_{2}$ $^{29}/_{2}$—$^{11}/_{3}$ $^{13}/_{5}$—$^{16}/_{5}$	$4 \times {}^{1}/_{4}$	54,000 18,000	5 2	40 5 6	0.44 Sn + 0.25 Cu + 1 Al 4 Pb. 6 Pb.	$^{20}/_{5}$ 1932	3 m.	3 d.
15. 576/32 Pr. Ca. of Lip 75 years ♂	1930 1931 1932	$^{28}/_{7}$ — $^{1}/_{8}$ $^{15}/_{8}$ —$^{20}/_{8}$ $^{29}/_{12}$— $^{3}/_{1}$ $^{3}/_{1}$ —$^{10}/_{1}$ $^{25}/_{2}$ — $^{3}/_{3}$	$3 \times {}^{1}/_{4}$	15,000 23,000 15,000 21,000	1 1 1 1	30 6 6 3 6	0.44 Sn + 0.25 Cu + 1 Al 6 Pb. 6 Pb. 4 Pb. 6 Pb.	$^{16}/_{6}$ 1932	2 y.	$3^{1}/_{2}$ m.
16. 883/32 Pr. Ca. of Lip 82 years ♀	1930	$^{5}/_{5}$—$^{19}/_{5}$	—	18,000	1	6	6 Pb.	$^{1}/_{11}$ 1932	$2^{1}/_{2}$ y.	$2^{1}/_{2}$ y.
17. 351/28 Pr. Ca. of Tongue 59 years ♂	1928	$^{26}/_{6}$— $^{2}/_{7}$ $^{16}/_{8}$	—	24,000 6,500	3 1	5 5	4 Pb. 4 Pb.	$^{17}/_{8}$ 1928	8 w.	1 d.
18. 60/29 Pr. Ca. of Tongue 50 years ♂	1928 1929	$^{11}/_{11}$–$^{18}/_{11}$ $^{16}/_{12}$–$^{19}/_{12}$ $^{26}/_{1}$— $^{1}/_{2}$	—	30,000 10.700 16,000	4 2 4	5 5 5	4 Pb. 4 Pb. 4 Pb.	$^{8}/_{2}$ 1929	3 w.	1 w.

Microscopic findings in the lymph nodes
In one node, apparently complete necrosis of all cancer cells with formation of a cyst filled with cornified debris and lined by giant cells of foreign body type and reticulo-endothelial cells; necrosis of smaller cancer nodules within the capsule, plasma cells +, degenerative blood vessel changes + (Fig. 3). In another node, same necrosis of cancer surrounded by wall of giant cells of foreign body type, but in addition strands of cancer cells with mitoses invading remainder of node, many tubercle-like areas, plasma cells + +, degenerative and proliferative blood vessel changes + + +, thickened capsule invaded by growing cancer.
Necrosis of most of cancer cells with formation of a cyst lined chiefly by giant cells of foreign body type and reticulo-endothelial cells but in some places by cancer cells; cyst filled with cornified debris and neutrophils; cords and strands of cancer cells in the lymphatic tissue external to the cyst, no mitoses, plasma cells + + +, eosinophils + +, some connective tissue formation, degenerative blood vessel changes + +.
Apparently necrosis of all cancer tissue leaving large cysts filled with cornified debris and lined by giant cells of foreign body type, fatty mononuclear phagocytes and reticulo-endothelial cells; most of the giant cells contain cholesterin crystals; plasma cells + +, much connective tissue formation in the node, many tubercle-like areas, degenerative blood vessel changes +, thickened capsule (Fig. 1).
Large areas of necrosis of cancer cells leaving cysts filled with cornified debris and neutrophils and surrounded by degenerating cancer, much connective tissue formation with scattered groups of degenerating cancer cells, plasma cells, neutrophils and eosinophils + + +, degenerative and inflammatory blood vessel changes + + +, capsule invaded by cancer cells.
In one node, apparently necrosis of all cancer tissue leaving only a thin capsule covering the cyst lined by giant cells of foreign body type and reticulo-endothelial cells and filled with cornified debris; proliferative and degenerative blood vessel changes + + +. Another node is similar but a few cancer cells remain, new subcapsular connective tissue contains a few plasma cells and neutrophils, degenerative blood vessel changes +, thickened capsule contains a few cancer cells.
Extremely large node with necrosis of large areas of cancer, numerous large cysts filled with cancer debris and neutrophils and lined by cancer cells which are growing out into the node in all directions, mitoses + +, a few plasma cells, neutrophils and eosinophils, degenerative blood vessel changes + +, invasion of capsule by cancer cells.
In one node the entire lymphatic structure is replaced by a rim of cancer cells surrounding a large cavity filled with neutrophils and an occasional cancer cell; degenerative blood vessel changes + +, capsule invaded by cancer cells and by eosinophils and neutrophils. In another node, the lymphatic structure is replaced by living cancer cells with moderate numbers of mitoses, plasma cells + + +, degenerative and inflammatory blood vessel changes +, capsule invaded by inflammatory and cancer cells.
Apparently complete necrosis of all cancer with formation of a cyst lined by giant cells of foreign body type and reticulo-endothelial cells and filled with cornified debris; a few plasma cells, many tubercle-like areas, degenerative blood vessel changes +.
Necrosis of large cancer masses with formation of cysts filled with cornified debris and surrounded by cancer cells, which are growing out in cords into the rest of the node, mitoses, much connective tissue formation, plasma cells + +, neutrophils + +, degenerative blood vessel changes + + +, thickened capsule invaded by cancer cells.

Case No. Biopsy No. Location Age Sex	Treatment								Time between first radiation and resection	Time between last radiation and resection
	Year	Date	Röntgen	Teleradium	No. of fields	Distance	Filter	Date of operation		
			HED	total mg hrs		cm	mm			
19. 439/29 Pr. Ca. of Tongue 59 years ♂	1929	17/9—27/9	—	34,000	3	5	4 Pb.	3/9 1929	2 w.	1 w.
20. 482/29 Pr. Ca. of Tongue 62 years ♂	1929	9/7—22/7	—	46,700	3	5	4 Pb.	10/9 1929	2 m.	7 w.
21. 252/31 Pr. Ca. of Tongue 60 years ♀	1931	17/1—21/1 19/1—24/1	—	36,000 20,000	3 2	6 5	6 Pb. 4 Pb.	19/3 1931	2 m.	7 w.
22. 959/32 Pr. Ca. of Tongue 60 years ♂	1932	24/3—8/4 1/6—8/6	—	100,000 18,000	5 1	5 6	4 Pb. 6 Pb.	7/6 1932	5 m.	3 m.
23. 460/30 Pr. Ca. of Bucca 49 years ♂	1930	26/1—2/2 23/4—24/4	—	37,300 30,000	3 3	5 6	4 Pb. 6 Pb.	2/6 1930	4 m.	6 w.
24. 552/32 Pr. Ca. of Bucca 48 years ♂	1932	31/3—6/4 9/5—10/5	—	50,000 52,000	5 3	5 6	4 Pb. 6 Pb.	18/5 1932	2 m.	2 d.
25. 1134/32 Pr Ca. of Bucca 72 years ♂	1932	29/4—3/5 19/7—27/7	—	48,000 47,300	3 2	6 6	6 Pb. 6 Pb.	6/10 1932	6 m.	10 w.
26. 62/28 Pr. Ca. of Vulva 68 years ♀	1927 1928	5/10—8/10 24/11—27/11 4/2—5/2	4 × 1/2	32,000 18,000	5 3	40 5 5	0.5 Cu × 1 Al 4 Pb. 4 Pb.	10/2 1928	4 m.	5 d.
27. 205/28 Pr. Ca. of Vulva 66 years ♀	1928	1/2—3/2 29/4—2/5	2 × 1/2	21,000	2	50 5	0.5 Cu + 1 Al 4 Pb.	11/5 1928	3 m.	9 d.
28. 216/28(l) [1] Pr. Ca. of Vulva 71 years ♀	1928	4/4	1	—	—	30	0.44 Sn + 0.25 Cu + 1 Al	24/5 1928	2 m.	4 w.
(r) [1] Pr. Ca. of Vulva	1928	5/4—30/4	—	20,000	1	5	4 Pb.	»	2 m.	3 w.
29. 359/29 Pr. Ca. of Vulva 64 years ♀	1929	23/4—25/4	4 × 1/2	—	—	40	0.5 Cu + 1 Al	30/7 1929	12 w.	12 w.
30. 709/30 Pr. Ca. of Vulva 71 years ♀	1930	20/6—25/6 27/6—1/7	4 × 1/2	13,600	2	40 5	0.44 Sn + 0.25 Cu + 1 Al Pb.	18/6 1930	2 m.	7 w.

[1] l = left inguinal nodes.
r = right inguinal nodes.

Microscopic findings in the lymph nodes
Many degenerating cancer cells, one small cyst filled with fluid and lined by non-cornifying cancer epithelium; many mitoses, few plasma cells, eosinophils + +, neutrophils +, much loose connective tissue, degenerative blood vessel changes +, capsule thickened and invaded by cancer cells.
Massive necrosis of large areas of cancer cells leaving cysts filled with cornified debris and lined by cancer epithelium; a few plasma cells, eosinophils +, many tubercle-like areas, degenerative blood vessel changes + (Fig. 8).
No necrosis, cancer masses lying in young connective tissue, very little lymphatic tissue remains, no mitoses and considerable degeneration of cancer cells, plasma cells + +, degenerative blood vessel changes +.
Apparently complete necrosis of cancer leaving only the lymph node capsule, a very few lymphocytes and the rest of the node replaced by connective tissue and a fluid filled cyst with no epithelial lining, a few plasma cells, degenerative blood vessel changes +, thickened capsule (Fig. 2).
Necrosis of cancer tissue leaving cysts lined by cancer cells and containing small amounts of cornified debris; strands of cancer cells outside the cyst wall invading the capsule, almost no plasma cells, considerable connective tissue formation, degenerative blood vessel changes +.
Apparently complete necrosis of cancer leaving only a cyst filled with cornified debris and lined by giant cells of foreign body type and reticulo-endothelial cells; plasma cells + +, much connective tissue formation, many tubercle-like areas, degenerative blood vessel changes +.
Necrosis of large masses of cancer leaving a cyst lined by cancer cells; much connective tissue formation and many strands of cancer cells throughout, very few mitoses, many giant cells of foreign body type, a few plasma cells, degenerative blood vessel changes + + +, thickened capsule.
Large areas of necrosis leaving fluid filled cysts lined by cancer cells; other masses of cancer cells surrounded by dense connective tissue, many mitoses, plasma cells + + +, very much thickened capsule containing many young capillaries, no blood vessel changes.
Necrosis of large masses of cancer with formation of masses of cornified debris surrounded by cancer cells which are invading the node and contain many mitoses; considerable connective tissue formation, plasma cells + + +, no blood vessel changes, invasion of the capsule by cancer cells.
Large areas of necrosis of cancer tissue leaving cysts filled with cornified debris and lined by cancer cells which are growing out into the lymphatic tissue, many mitoses, plasma cells +, considerable connective tissue formation, no blood vessel changes, invasion of capsule by cancer cells.
Exactly the same picture.
Necrosis of larger cancer masses leaving cysts filled with cornified debris and lined by cancer cells, no mitoses in the strands of cancer cells outside the cysts, plasma cells very few, eosinophils + + +, no blood vessel changes, invasion of capsule by cancer.
Very few cancer cells, all degenerating, some connective tissue formation, a few plasma cells, no blood vessel changes, capsule invaded by cancer.

Case No. Biopsy No. Location Age Sex	Treatment								Time between first radiation and resection	Time between last radiation and resection
	Year	Date	Röntgen	Teleradium	No. of fields	Distance	Filter	Date of operation		
			HED	total mg hrs		cm	mm			
31. 502/31 Pr. Ca. of Vulva 42 years ♀	1931	28/3—6/4	—	30,600	2	5	4 Pb.	1/6 1931	10 w.	2 m.
32. 1074/31 Pr. Ca. of Vulva 26 years ♀	1931	16/10–23/10	—	60,000	2	5	4 Pb.	2/12 1931	7 w.	6 w.
33. 1086/31 Pr. Ca. of Vulva 63 years ♀	1931	29/9—6/10	—	30,000	2	6	6 Pb.	8/12 1931	10 w.	2 m.
34. 73/32 Pr. Ca. of Vulva 69 years ♀	1929	5/8—10/8 8/12—4/12	—	20,000 10,000	1 1	5 5	4 Pb. 4 Pb.	27/1 1932	2½ y.	2½ y.
35. 250/32 Pr. Ca. of Vulva 56 years ♀	1931 1932	26/12—24/1 25/1—24/1	—	18,000 13,000	2 2	6 5	6 Pb. 4 Pb.	8/3 1932	15 w.	2 m.
36. 1579/32 Pr. Ca. of Vulva 71 years ♀	1931 1932	17/10–25/10 11/11–13/11 19/11–13/11	—	30.000 12,000 8,000	2 1 1	6 6 5	6 Pb. 6 Pb. 4 Pb.	1/12 1932	11 m.	10 d.
37. 68/31 Pr. Ca. of Penis 66 years ♂	1930	14/10–18/10 29/11–30/11	2 × ½	21,000	2	40 6	0.5 Cu + 1 Al 6 Pb.	15/1 1931	2½ m.	6 w.
38. 1658/32 Pr. Ca. of Penis 64 years ♂	1931	30/4—7/5 6/7—13/7	3 × ½ 3 × ½	—	—	30 30	0.44 Sn + 0.25 Cu + 1 Al 0.44 Sn + 0.25 Cu + 1 Al	15/12 1932	19 m.	16 m.
39. 225/28 Pr. Ca. of Anus 73 years ♀	1928	13/4—24/4	—	28,000	3	5	4 Pb.	1/6 1928	3 m.	7 w.
40. 226/28 Pr. Ca. of Anus 57 years ♀	1927 1928	27/12 17/2—22/2 19/4—24/4	3 × ½ 3 × ½	7,000	1 1 1	5 40 40	4 Pb. 0.5 Cu + 1 Al 0.5 Cu + 1 Al	1/6 1928	4 m.	1 w
41. 1093/30 Pr. Ca. of Anus 57 years ♂	1930	20/10–22/10	—	30,000	2	6	6 Pb.	12/2 1931	8 w.	8 w.

Microscopic findings in the lymph nodes
Necrosis of large cancer masses leaving a cyst filled with fluid and small amounts of cornified debris and lined by cancer cells; a few mitoses in groups of cancer cells outside the cyst, plasma cells + +, some connective tissue formation, degenerative blood vessel changes + +, capsule invaded by cancer.
Apparently complete necrosis of cancer leaving a solid mass of cornified material surrounded by reticulo-endothelial cells and a few giant cells of foreign body type; a few plasma cells, no blood vessel changes.
Several nodes containing large masses of necrotic cornified cancer surrounded by cancer cells; large masses of partially injured cancer cells, no mitoses, plasma cells + + +, some giant cells of foreign body type, degenerative and proliferative blood vessel changes + +, thickened capsule invaded by cancer cells.
Large areas of necrotic and injured cancer tissue, very few mitoses, much connective tissue formation, no cellular reaction, degenerative blood vessel changes + + +, invasion of capsule by cancer tissue.
Necrosis of cancer tissue with formation of masses of cornified debris surrounded by cancer cells which extend out into the node but show no mitoses, eosinophils + +, plasma cells + + +, a few giant cells of foreign body type, some connective tissue formation, degenerative blood vessel changes + + + (Fig. 14).
Necrosis of cancer masses with formation of cysts filled with cornified debris and lined by cancer cells; partially injured cancer cells scattered throughout the node, much connective tissue formation, giant cells of foreign body type and tubercle-like structures + +, plasma cells + + +, degenerative blood vessel changes +, invasion of capsule by cancer.
Necrosis of an extremely large cancer mass leaving a large cyst filled with cornified debris and lined by cancer cells which are growing out in cords into the node, moderate numbers of mitoses, plasma cells + +, a few tubercle-like areas and giant cells of foreign body type, no definite blood vessel changes, capsule invaded by cancer cells.
Necrosis of many cancer masses leaving cysts filled with cornified debris and lined by cancer cells; large areas of growing cancer with mitoses, a few eosinophils and plasma cells, no blood vessel changes, invasion of the capsule by cancer.
Large areas of necrotic cancer leaving cysts filled with cornified debris and lined by cancer cells; other areas of growing cancer with mitoses, plasma cells + +, neutrophils +, no blood vessel changes, capsule thickened and invaded by cancer cells.
Large areas of necrotic cancer leaving cysts filled with cornified debris and lined by cancer cells; other areas of growing cancer with mitoses, some connective tissue formation, plasma cells +, neutrophils + +, degenerative blood vessel changes + +, cancer cells growing within a large blood vessel in the capsule, capsule thickened and invaded by cancer.
Necrosis of very large areas of cancer leaving cysts filled with cornified debris and lined by cancer cells; many other areas of partially injured cancer cells, a few mitoses, a few tubercle-like areas and giant cells of foreign body type, plasma cells + +, degenerative blood vessel changes + +, necrosis of capsular invasion in one node.

cancer cells. In order to investigate the origin of these giant cells of foreign body type, five different stains were used (hematoxylin-eosin, van Gieson, Giemsa, Mallory phosphotungstic acid hematoxylin and Bielschowsky) on each of nine blocks of tissue. The Lipchütz stain could not be used because the tissues were formalin fixed.

The material consisted of (1) two pieces of tissue containing a foreign body and foreign body giant cells, (2) an epulis, (3) a tuberculous lymph node with many giant cells, (4) an osteogenic sarcoma with tumor giant cells, and (5) four of the radiated lymph nodes containing large numbers of giant cells of the foreign body type. On examination of these sections no differences could be detected between the staining of known foreign body giant cells, tuberculous giant cells not of the Langhans type, epulis giant cells and the giant cells of the foreign body type in these cancerous lymph nodes.

These latter giant cells seemed to be derived from the reticulo-endothelial cells of the node or from fatty mononuclear phagocytes. In several nodes all transition stages could be seen between the mononuclear phagocytes and the adjacent giant cells. The nuclei and the structure of the protoplasm were identical. Both the mononuclear phagocytes and the giant cells were always found beside necrotic cornified material. Many of the giant cells contained masses of this cornified debris as well as cholesterin crystals and leucocytes. The protoplasmic processes of many of the giant cells seemed to be continuous with the processes of the parenchymal cells of the node. With the silver stain reticulum fibrils could be seen entering the periphery of these giant cells. Not a single mitosis was observed in any of them.

When one considers the lack of agreement as to the origin of the giant cells in untreated giant cell tumors in the ends of the long bones (Lacharite) the still greater difficulty of absolutely proving the origin of these cells in a radiated cancerous lymph node becomes apparent. The solution is made more difficult because we do not know the effect of radiation on foreign body giant cells. It would seem possible that their nuclei or protoplasm would show signs of injury but such was not the case. The giant cells of the foreign body type had exactly the same appearance in the non-radiated as in the radiated nodes. Neither do we know whether radiation can partially injure cancer cells and cause them to resemble foreign body giant cells. The chief importance of the matter lies in the possibility of recurrence from such cells if they are of tumor origin. For example, in 11 of the radiated lymph nodes under discussion there remained after radiation only giant cells of the foreign body type and no definitely recognizable cancer cells.

The evidence obtained in this investigation shows that these cells have the same origin and morphology as known foreign body giant cells.

4) *The blood vessels.* There were definite pathological changes in the blood vessels in 28 of the 41 cases and in 17 of these the lesions were graded ++ or +++. No abnormalities of the vessels were found in the other 13 cases in spite of the examination of numerous sections. In 14 cases the biopsy material contained both cancerous and non-cancerous lymph nodes. Sections of the latter showed no blood vessel changes even in the 4 cases where the adjacent cancerous nodes contained strikingly abnormal vessels (4, 7, 14 and 35). The nine cases of cancer with suspected metastases, where the lymph nodes were radiated and removed and no cancer found, showed no blood vessel lesions in these nodes. In the control group of 17 non-radiated cancerous nodes there were definite vascular changes in only 1 case.

One node from case 10 removed 16 days after the first and 11 days after the last radiation showed changes in the vessels but otherwise the most extensive lesions were found in nodes taken out 2 or more months after the last treatment. However, several of the inguinal nodes extirpated some months after radiation seemed to have absolutely normal blood vessels. The lesions were often just as marked in nodes where the cancer was actively growing (34, 35) as in nodes where there was extensive necrosis (18).

The most marked lesions were found in the small and medium-sized arteries. The larger arteries rarely exhibited any changes and then only in the presence of massive necrosis (5). No capillary lesions were found but none of these nodes were removed in less than 2 weeks after the first radiation. The seven nodes (1, 17, 18, 19, 24, 26 and 40) which were removed in less than 7 days after the last treatment had all had previous radiation which may have complicated the picture. The vessels most affected were those in the capsule and in the connective tissue around the cancer. Vessels out in the hilus rarely showed any abnormality.

A comparison with the blood vessels of normal lymph nodes showed that the small and medium-sized arteries in $^2/_3$ of these cancerous radiated nodes had become very conspicuous. They were prominent even under low power because of the small size of the lumen in comparison to the thickness of the wall. The latter was swollen and seemed to be undergoing some type of hyaline degeneration which involved the subendothelial and the inner part or all of the muscle layer (Fig. 12 and 14). There were fewer nuclei than normal and many of them were degenerating. The hyalinization did not always extend uniformly around the vessel but might be found on only one side. The hyaline material stained red with eosin and yellow with van Gieson. There was a fatty degeneration of the subendothelial connective tissue where the cells were enormous and filled with fat. This fatty degeneration sometimes involved the muscle layer as well.

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In 4 cases there were marked proliferative changes throughout the vessel walls but particularly internal to the internal elastic membrane (Fig. 10, 11 and 15). The latter structure appeared normal but internal to it the subendothelial connective tissue had proliferated until the the lumen of the vessels was extremely small and the wall very thick and cellular. The node showing perhaps the most marked degenerative and proliferative changes in many vessels was 34 removed 2½ years after treatment with the cancer growing vigorously throughout.

In lymph nodes with large areas of necrosis there were sometimes quite large vessels which had apparently been partially thrombosed and then recanalized. In such cases the lumen was eccentric and very small and the subendothelial connective tissue contained considerable fat (Fig. 15). There were also a few acute thromboses of larger vessels on the edge of necrotic cancer masses. On the other hand there were only very slight or no blood vessel changes to be found in many cases with massive cancer necrosis (6, 8, 9, 14, 37, 39 and 41).

With reference to the effect of radium or röntgen on blood vessels, 8 of the 17 cases with marked pathological vascular changes had received radium only, 2 röntgen only and the other 7 both röntgen and radium.

5) *The capsule.* Almost all of the cervical and inguinal nodes in this series possessed a definite capsule. In the 41 nodes containing cancer or cancer remnants, the capsule was often thicker than normal and when blood vessel changes of either proliferative or degenerative type were present they could be best studied in the capsule. Occasionally lymphatic and plasma cell infiltration was seen around the small vessels. In a few cases macrophages and connective tissue cells filled with blood pigment could be found in the capsule, thus suggesting the possibility of previous thrombosis or capillary hemorrhage. Although a margin of lymphatic tissue usually separated the capsule from the cancer, in three cases at least there seemed to be only a rim of giant cells or nothing at all between the two, over long distances (10, 14 and 41).

The capsule was invaded by cancerous tissue in 22 of the 41 cases. These cancer masses may have been resistant to radiation or they may have developed since the last treatment. There were 2 cases however, where these intracapsular cancer nodules had been reduced to complete necrosis and were surrounded by a wall of giant cells of the foreign body type and connective tissue cells.

Discussion

As far as could be judged from a very great number of sections of each specimen, nodes from 11 cases (7 lip, 2 tongue, 1 bucca and 1 vulva) showed *apparently complete destruction of the cancer cells* (Fig. 1, 2 and 3).

Nothing of the cancer remained except an empty cavity or a cavity containing necrotic cornified material and lined by giant cells of the foreign body type. The time intervals between the first radiation and the removal of these nodes were as follows: 16 days, 3 weeks, 1 month, 6 weeks, 7 weeks, 7 weeks, 8 weeks, 2 months, 3 months, 4 months and 5 months. The histological picture in the first 10 cases was identical. The necrosis, degeneration and disappearance of the cancer tissue was just as complete in the two nodes removed 2 and 3 weeks after treatment as in those removed later. In node 22 removed 5 months after the first and 3 months after the last treatment, the node was so completely healed that only a small fluid-filled cavity remained with connective tissue walls and an occasional giant cell of the foreign body type. The node parenchyma was almost completely replaced by connective tissue. In 4 of the 11 cases, an adjacent node removed at the same time showed only partial necrosis of the cancer. These 4 nodes were not larger nor was the metastasis itself larger than in the adjacent nodes where the cancer had completely disappeared. 9 of these 11 cases had had definitely more radiation than the average. In 8 of the 11 nodes there had been excessive keratosis recognizable from the shadow remnants in the necrotic cavities. None of the non-radiated cancerous lymph nodes showed complete necrosis of all cancer tissue.

23 nodes contained *large areas of cancer necrosis lined by cancer epithelium.* In many cases a large or small part of the cyst wall was formed by giant cells. In about $^2/_3$ of this group the cystic areas were filled with the necrotic remnants of hyperkeratotic masses of cancer cells. In $^1/_3$ of the group the cyst contained only fluid and a very few dead inflammatory and epithelial cells. In such cases there was less cornification in the cancer of the rest of the node and also less giant cell reaction. The lesions seen in the cancer tissue of the lymph nodes in this group are exactly duplicated in a few of the non-radiated cancerous lymph nodes (Compare Fig. 4 and 5). The latter also contained fluid filled cysts lined with cancer epithelium, large necrotic cysts lined completely or partially by either giant cells or cancer tissue or both and even, but not as frequently, the small foreign body tubercles around very small masses of necrotic cancer. In these non-radiated nodes, however, there were usually, but not always, more mitoses.

It was impossible to study the early stages of *cancer necrosis* in these nodes since so many were removed over 3 weeks after radiation. However at the time of extirpation the necrotic material in 31 nodes was clearly derived from cornified cancer cells. There were 7 nodes (2, 16, 19, 22, 25, 26 and 31) where the cystic cavities contained only fluid and a few inflammatory or cancer cells. There were 2 nodes (15 and 34) which contained very large areas of cancer necrosis with almost no cornification

but these were removed 2½ years and 3 months respectively after the last radiation. There were two other nodes (4 and 30), both extirpated about 6 weeks after the last treatment where all the cancer cells were injured but there was almost no sign of cornification. A comparison with the non-radiated cancerous nodes shows that in one of these there is necrosis without cornification, in three there are cystic cavities containing fluid, an occasional cell and no cornified material and in the remaining 15 the cystic necrotic cavities are filled with cornified debris.

The primary tumors of most of these lymph node metastases were available but a great number of them had been radiated before the biopsy was done. It was therefore impractical to grade them. In the non-radiated primary tumors no correlation could be found between the histological structure and the tendency of the metastasis to excessive cornification or to cyst formation under the influence of radiation. Some of the primary tumors with much cornification had produced metastases with almost none and vice versa.

Three of the inguinal nodes in this series contained, in addition to the cancer metastasis, *large hyaline nodules almost entirely replacing some of the germinal centers* (28, 35 and 38). Three of the non-cancerous radiated inguinal nodes from cases of cancer showed the same picture. These hyaline masses were almost completely acellular except for a few areas of finely granular material which stained blue with hematoxylin and could be suspected of being nuclear remnants. The hyaline masses stained red with van Gieson and could not be shown to be remnants of degenerated cancer. Areas such as these were not seen in any of the non-radiated cancerous nodes.

Giant cells of the foreign body type were always found in radiated and non-radiated nodes wherever necrotic cancer came directly in contact with lymph node tissue. Where the necrotic cancer was surrounded by living cancer cells, no giant cells formed. The most marked giant cell reaction was seen in the cervical nodes. Nodes removed 2 weeks after radiation and nodes removed 5 months after, still contained quantities of these cells. Foreign body giant cells were very much less frequent in inguinal nodes, both radiated and non-radiated. The presence of these giant cells must be regarded as a favorable sign. They completely walled off the areas of necrosis in the 11 nodes where no living cancer cells could be found. They occurred in very small numbers or not at all in nodes where the cancer was progressing. Cancer cells were never seen growing out into the node through a wall of giant cells of the foreign body type.

There was an *acute or subacute inflammatory process* in 6 nodes of this series (4, 11, 13, 18, 37 and 40). Five of these contained large areas of necrosis but the carcinoma was still proliferating. In no case was there

complete necrosis of the cancer in the presence of inflammation in the node.

Two thirds of the radiated cancerous lymph nodes showed *changes in the blood vessels*. The most marked lesions were seen in the small and medium sized vessels of nodes removed about 2 months or more after radiation. The blood vessel changes seem to be dependent on the presence of cancer in the node since there were no vascular lesions in the radiated non-cancerous nodes removed in the same group with cancerous nodes which did show vascular lesions. Most of these nodes had undergone extensive necrosis but the lesions in the vessels were not only dependent on the necrosis because several of the non-radiated nodes contained just as large areas of necrotic cancer and there were no blood vessel changes. None of the eleven nodes where there was apparently complete death of all cancer cells, showed very marked vascular lesions and one of the non-radiated cancerous nodes showed slight but definite lesions. In view of such facts the blood vessel changes observed in these nodes cannot be said to have caused much of the cancer degeneration although they may have contributed to it.

There was no difference in the amount or degree of vascular change following radium and röntgen treatment. In case 28 where the left inguinal nodes were given röntgen and the right inguinal nodes radium the histological picture was exactly the same in all respects.

The author wishes to thank Professor H. BERGSTRAND of Sabbatsberg Hospital, Stockholm, Professor F. B. Mallory of Harvard Medical School and Professor E. T. BELL of the University of Minnesota for part of the non-radiated tissues used in this study.

SUMMARY

The histological changes in these 41 radiated cancerous lymph nodes were also to be found, although to a lesser degree, in some of the non-radiated cancerous nodes.

Although two-thirds of the radiated and only one non-radiated node showed degenerative and proliferative vascular lesions in the small arteries, these changes did not seem to precede and did not parallel the extent of the cancer necrosis or the amount of radiation and they cannot be said to be more than contributory to the death of the cancer.

The cancer was apparently completely destroyed in 11 of the radiated nodes.

The lymphatic tissue at the time of resection of these nodes seemed to be uninjured by the röntgen and radium treatment and it was quite impossible to determine histologically whether the non-cancerous nodes had been radiated.

No histological differences were observed in the reaction of the blood vessels, cancer cells or lymphatic tissue to röntgen or to radium treatment.

ZUSAMMENFASSUNG

Die konstatierten histologischen Veränderungen in 41 bestrahlten karzinomatösen Lymph-knoten wurden auch, wenngleich in geringerem Grade, in einigen von den nicht bestrahlten karzinomatösen Knoten gefunden.

Obgleich zwei Drittel der bestrahlten und nur ein nicht bestrahlter Lymph-knoten degenerative und proliferative vaskulare Läsionen in den kleinen Arterien zeigten, schienen diese Veränderungen der Karzinomnekrose nicht vorauszugehen und nicht mit der Ausdehnung der Karzinomnekrose oder der Bestrahlungsdosis parallel zu gehen. Man kann nicht sagen, dass sie mehr als eine beitragende Ursache für die Abtötung des Karzinoms wären.

In 11 von den bestrahlten Lymph-knoten war das Karzinom offenbar vollständig zerstört.

Das Lymphgewebe schien zur Zeit der Resektion dieser Knoten keine Schädigung durch die Röntgen- und Radiumbehandlung erlitten zu haben, und es war ganz unmöglich histologisch zu entscheiden, ob die nicht karzinomatösen Knoten bestrahlt worden waren.

Betreffs der Reaktion der Blutgefässe, Karzinomzellen oder des Lymphgewebes auf die Behandlung waren keine histologischen Unterschiede zwischen den mit Röntgen- und den mit Radiumbestrahlten Drüsen zu beobachten.

RÉSUMÉ

Les modifications histologiques dans ces 41 nodules lymphatiques cancéreux irradiés se retrouvaient également, bien qu'à un moindre degré, dans un certain nombre de nodules cancéreux non irradiés.

Bien que les deux tiers des nodules lymphatiques irradiés et un seul des nodules non-irradiés présentassent des lésions vasculaires dégénératives et prolifératives au niveau des petites artères, ces lésions ne semblent pas préétablies, et ne sont parallèles ni à l'extension de la nécrose du cancer ni à la dose d'irradiation; elles ne peuvent qu'être considérées comme contribuant à la mort du cancer.

Le cancer paraissait complètement détruit dans 11 des nodules lymphatiques irradiés.

Au moment de la résection des nodules, le tissu lymphatique ne paraissait avoir souffert ni du traitement radiothérapique ni de la curiethérapie, et il était tout à fait impossible d'établir histologiquement si les nodules non-cancéreux avaient été irradiés.

On n'a noté aucune différence dans la réaction des vaisseaux sanguins, des cellules cancéreuses ou du tissu lymphatique, entre la radiothérapie et la curiethérapie.

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Plate I.

Fig. 1. Case 12. Cervical metastasis from cancer of the lip. Resection one month after the first and only radiation. Röntgen only. Apparently complete necrosis of all cancer tissue. Cysts lined by giant cells of the foreign body type. Blood vessel changes +. × 7.

Fig. 2. Case 22. Cervical metastasis from cancer of the tongue. Resection 5 months after the first and 3 months after the last radiation. Radium only. Apparently complete death of all cancer tissue and replacement by connective tissue and a fluid-filled cyst. Blood vessel changes +. × 7.

Fig. 3. Case 10. Cervical metastasis from cancer of the lip. Resection 16 days after the first and 9 days after the last radiation. Chiefly röntgen. Apparently complete necrosis of all cancer tissue. Cyst lined by giant cells of the foreign body type. Blood vessel changes +. × 7.

Plate II.

Fig. 4. Case B. Area from a non-radiated cervical cancerous lymph node. Cyst containing necrotic cornified epithelium and lined by giant cells of the foreign body type. Apparently complete death of all cancer tissue. × 57.

Fig. 5. Case 6. Area from a radiated cancerous cervical lymph node. Resection 3 weeks after the first and 2 weeks after the last radiation. The microscopic picture is identical with that in Fig. 4. × 57.

Plate III.

Fig. 6. Case 12. Foreign body tubercle formed around minute masses of necrotic cancer in a cervical lymph node. The same case as Fig. 1. Giant cells of the foreign body type are surrounded by and attached to the hypertrophied reticulo-endothelium of the node. × 250.

Fig. 7. Case 8. Giant cell of the foreign body type from a cervical lymph node. To the left and above there is granular necrotic cornified tissue. To the right and below the giant cell is attached to the reticulo-endothelial cells of the node. × 350.

Plate IV.

Fig. 8. Case 20. Small blood vessels from a cervical lymph node. Resection 2 months after the first and 7 weeks after the last radiation. Radium only. Leucocytes infiltrating the swollen and degenerated subendothelial tissue. Marked narrowing of the lumen. × 350.

Fig. 9. Case 40. Tumor giant cells from an inguinal lymph node. Resection 4 months after the first and one week after the last radiation. Radium + röntgen. One of the cancer cells has one large nucleus; another has several superimposed hyperchromatic nuclei. Compare with the nuclei of the giant cells of the foreign body type in Fig. 6 and 7. × 800.

Plate V.

Fig. 10. Case 7. Small blood vessel in a cervical lymph node. Resection 15 months after the first and 2 months after the last radiation. Röntgen + radium. Proliferation of subendothelial connective tissue cells with marked narrowing of the vascular lumen. × 350.

Fig. 11. Same case as Fig. 10. The Weigert elastic tissue stain shows that the cellular proliferation which narrows the lumen is internal to the internal elastic membrane. × 350.

Plate VI.

Fig. 12. Case 14. Small blood vessel from a cervical lymph node. Resection 3 months after the first and 3 days after the last radiation. Radium + röntgen. Marked degeneration and swelling of the subendothelial connective tissue where almost no nuclei are to be found. Narrowing of the lumen. × 350.

Fig. 13. Case 5. Large blood vessel from the cervical lymph node. Resection 7 months after the first and 5 months after the last radiation. Röntgen + radium. This vessel has obviously been thrombosed and recanalized. It lies on the border of a large cyst filled with necrotic cancer. × 170.

Plate VII.

Fig. 14. Case 35. Small vessels from an inguinal lymph node. Resection 15 weeks after the first and 2 months after the last radiation. Radium only. Marked degeneration and swelling of the subendothelial and inner muscular tissue with narrowing of the lumen. × 350.

Fig. 15. Case 2. Small vessels from a cervical lymph node. Resection $2^1/_2$ months after the first and 4 days after the last radiation. Röntgen + radium. Marked proliferation of the subendothelial connective tissue, large cells filled with fat. Extreme narrowing of the lumen. × 350.

Fig. 1.

Fig. 2.

Fig. 3.

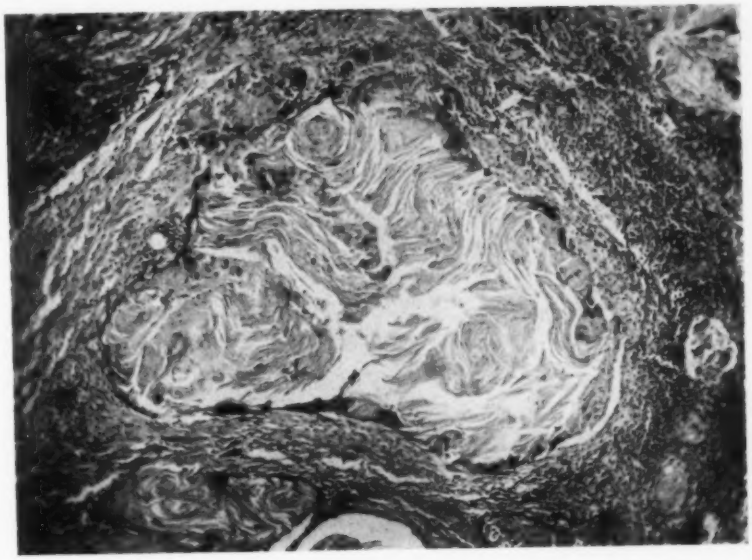

Fig. 4.

Fig. 5.

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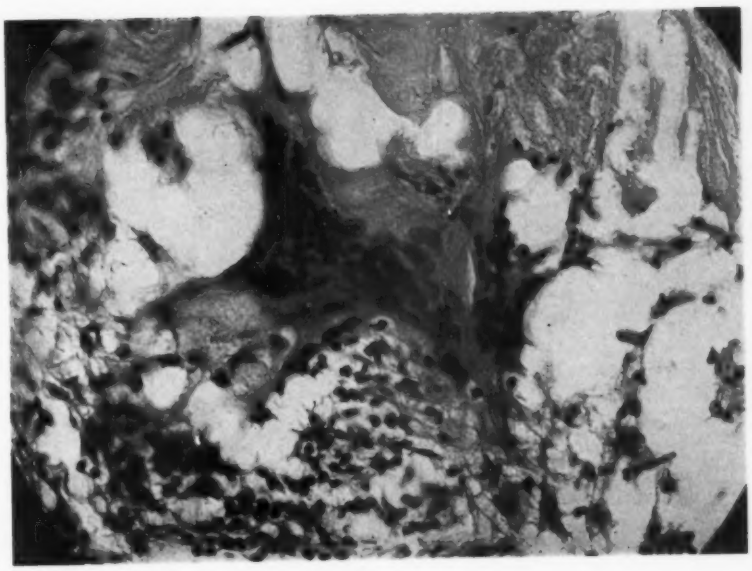
Fig. 6.



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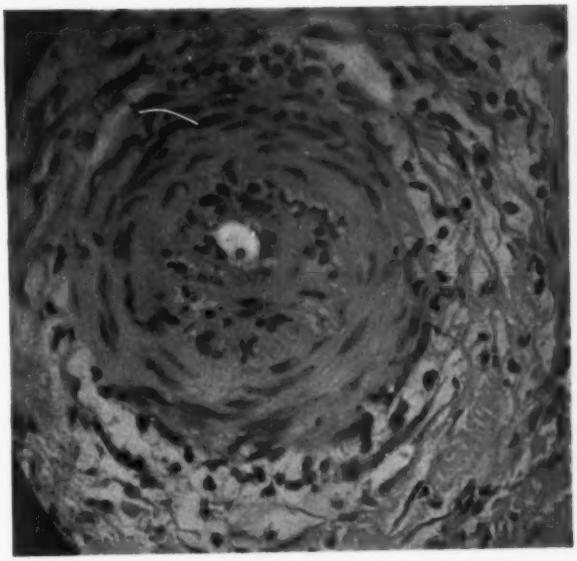

Fig. 8.

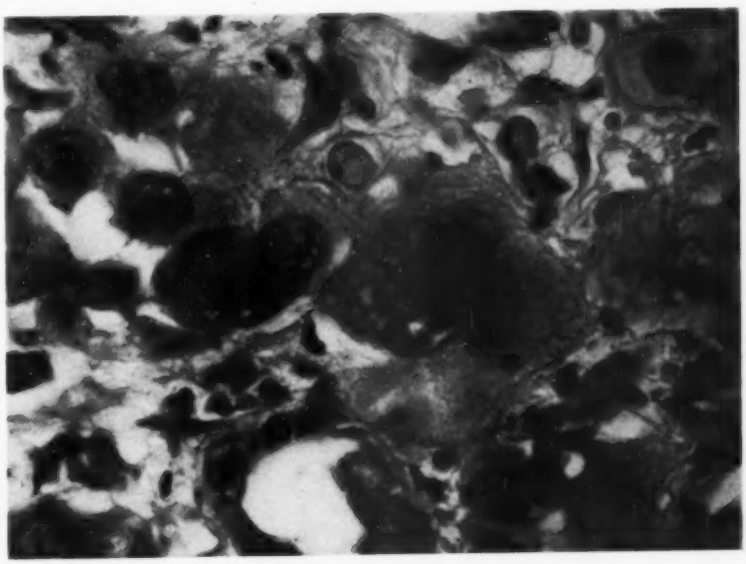

Fig. 9.

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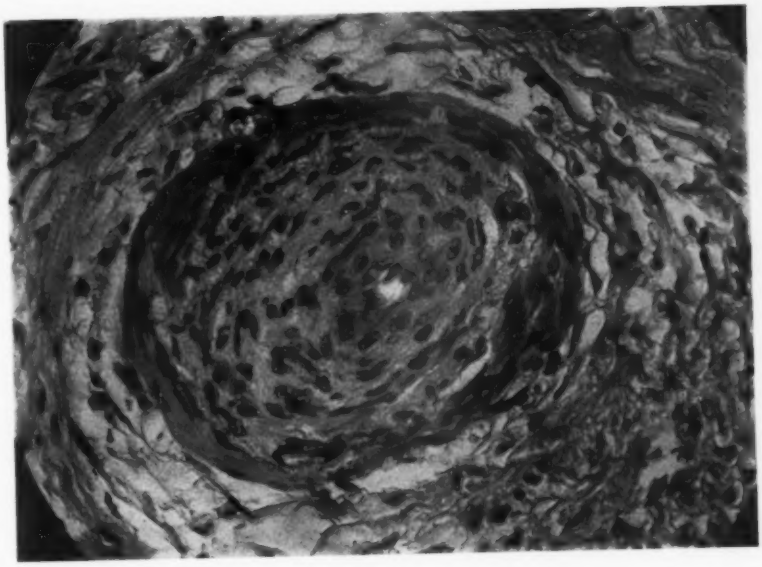

Fig. 10.

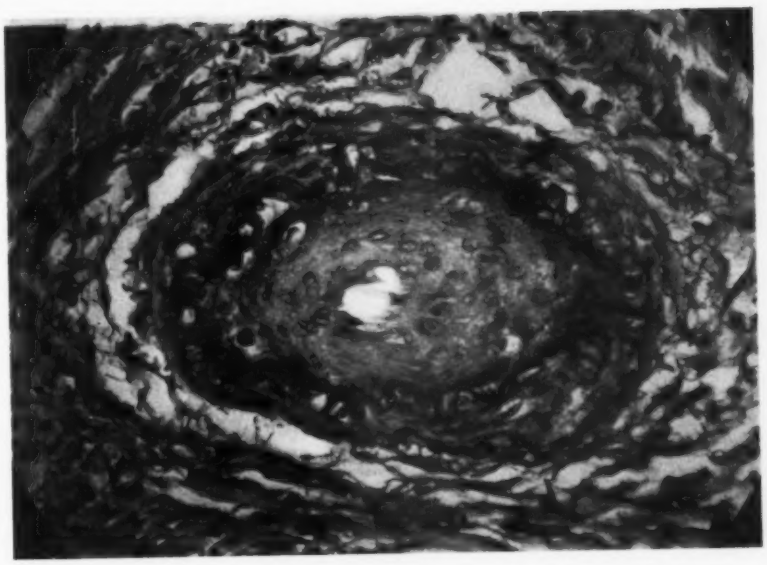

Fig. 11.

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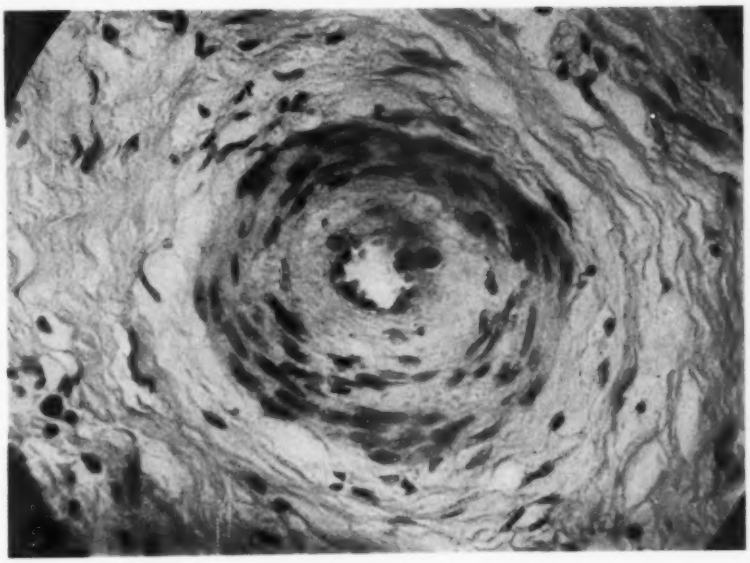

Fig. 12.

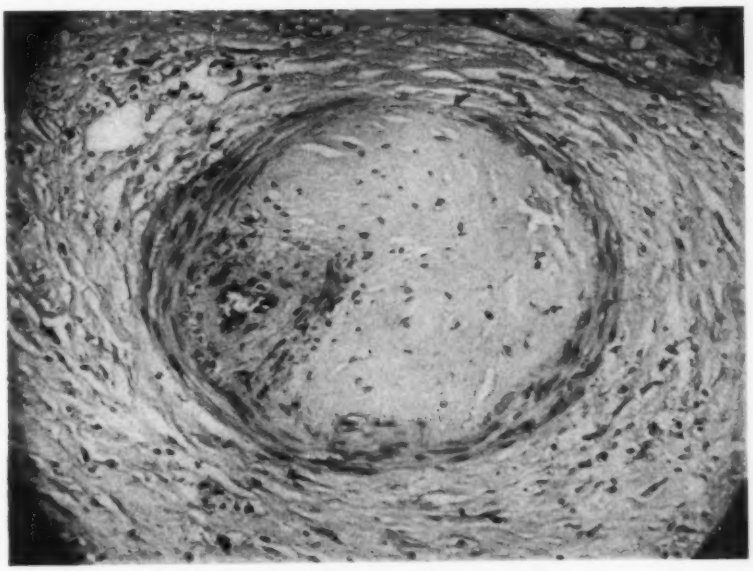

Fig. 13.

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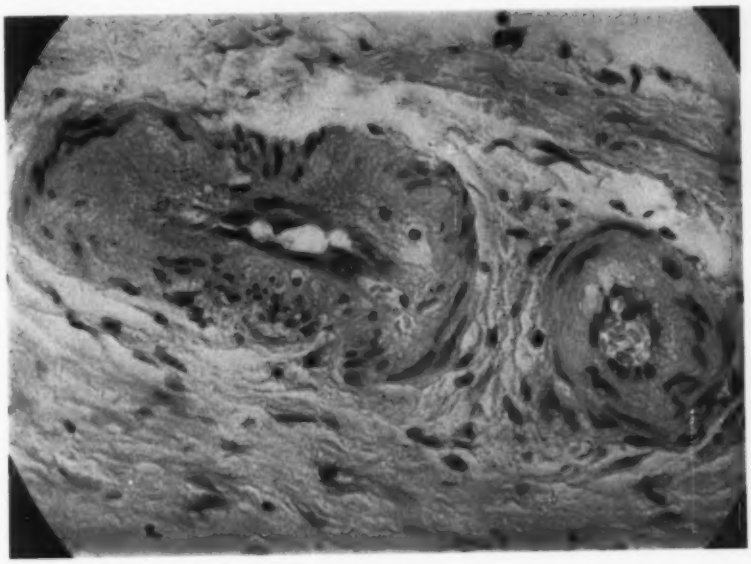

Fig. 14.

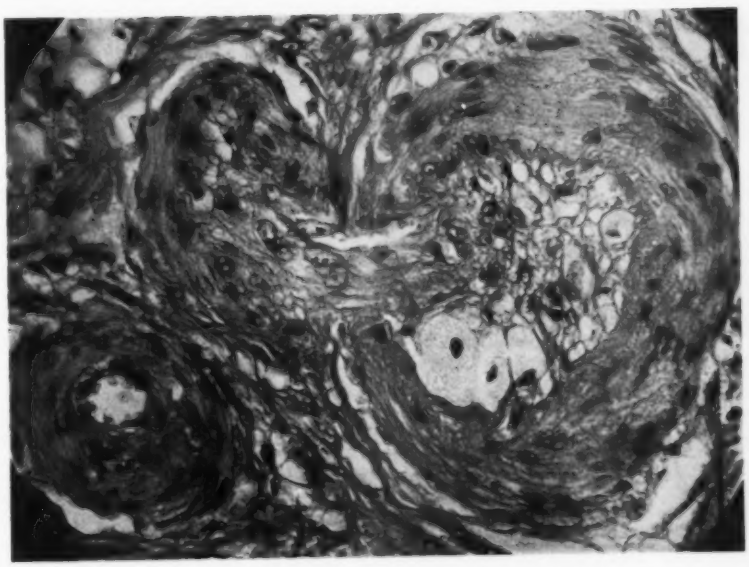

Fig. 15.

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FROM THE ROENTGEN DEPARTMENT OF THE KUNGL. AKADEMISKA SJUKHUSET, UPSALA.
CHIEF: PROFESSOR LAURELL

THE AXIAL TORSION[1] OF THE COLON THROUGH SO-CALLED PHYSIOLOGICAL VOLVULUS[2]

(An overlooked cause of obstruction in the enteric tube)

by

Karl-Erik Groth

(Tabulæ XXIX—XXX)

As is well known there are two different factors which constitute the syndrome of acute volvulus: obstruction of the passage of matter through the intestine and disturbance of the blood circulation in the twisted intestinal loop. Clinically, the condition presents a varying picture according to the degree with which either of these two factors take part. The majority of cases described in the literature on volvulus of the large intestine are characterized by an acute falling ill and a rapid development of a severe ileus condition. These cases have presented a complete occlusion of the intestinal passage and a more or less pronounced disturbance of the circulation in the twisted loop. The history of these cases generally gives the information that the patients have had periodical discomforts from the intestine, sometimes even for decennia. Under the name of *chronic*, *recurrent* or *atypic volvulus*, cases have been described which have proceeded more lingeringly under the picture of an obstinate constipation with meteorism and recurrent attacks of pain, conditions which can have lasted for weeks, sometimes with acute exacerbations and remissions (EDGREN, SCHAANING, BRAUN-WORTHMANN, BLOODGOOD, FURBER, MAZZINI, LIGAT-OVEREND, and others). In EDGREN's collection, out of 148 cases of S-volvulus, about 15 % were of this type. Some cases of atypic volvulus of the colon have had, besides meteorism, also rectal haemorrhages and diarrhoeas (KÜTTNER, KLINDT, BONNIOT, FURBER, ROWLANDS, LIGAT-OVEREND). LAURELL, who has

[1] By this term is understood, in the following, a torsion around the longitudinal axis of the intestine.

[2] Submitted for publication Jan. 27th, 1934.

devoted a close study to this atypic volvulus, has also described cases where meteorism is totally absent and the symptoms have consisted only of copious rectal haemorrhages or of diarrhoeas with or without admixture of blood. In those cases the intestinal passage evidently has not been completely occluded. LAURELL has interpreted these symptoms as expressions of strangulation of the vessels caused by the twisting. Against the opinion prevailing before, LAURELL emphasizes that this atypic volvulus is probably not uncommon, but that the majority of cases are not diagnosticated and registered, because they are spontaneously restored, sometimes after a rectal enema. Thus, it is evident, that *the syndrome of volvulus can be extremely variable, and that the violently acute cases have generally had previous symptoms which can be explained as slight attacks of volvulus.*

According to unanimous testimonies in the literature, the diagnosis »volvulus» is often extremely difficult to make clinically, and this is especially the case in atypic and mild cases, and in children, (BELLE). Radiological examination with and without opaque substance seems in this case to be very elucidative, and generally makes possible a positive diagnosis, (LAURELL, HINTZE, FERNSTRÖM, KLEINSCHMIDT, MONDOR, LIGAT-OVEREND, and others).

It is an old experience that the twisting of a loop of the large intestine up to 180° does not necessarily bring on signs of volvulus, (WILMS). On radiological examination of the colon with opaque enema, such twistings up to 180° are an extremely common finding (LAURELL), which is generally not associated with the symptoms from the intestine. This condition is known as *physiological volvulus.* Even a torsion of not more than 180° may give rise to obstruction of the passage of the faecal matters and disturbance of the circulation caused by compression at the foot point of the twisted loop. This is especially the case when there are cicatrizing processes in the mesosigmoid. It has also been assumed that passage obstruction in a twisted sigmoid loop could arise, if the afferent loop half lies behind a scybala-filled rectal efferent half and is steadily squeezed in the angle between this rectal half and the posterior abdominal wall.

An obstruction of the intestinal passage by so-called physiological volvulus can, however, apparently arise *even without the existence of such special conditions.* A series of observations from the Roentgen Department at Upsala on volvulus of the sigmoid as well as of the transverse colon favours the supposition *that the axial torsion of the intestine, which is always brought on by the twisting of a colon loop around its mesenteric axis, may sometimes be the cause of a local intestinal obstruction, and that in this case, the stenosed part does not always belong to the twisted loop, but may be found at some distance from the crossing point, either in oral or*

aboral direction. Owing to this fact the change is easily overlooked or misinterpreted at the examination.

That the loop parts in volvulus are twisted around their longitudinal axis at the crossing point has been emphasized, by LORENZ among others, but the importance of the axial torsion in volvulus has not been analysed in the literature as far as I have been able to find. An investigation into this question is the purpose of this publication. I pass over the mechanism for the genesis of the twisting of the *colonic loop around its*

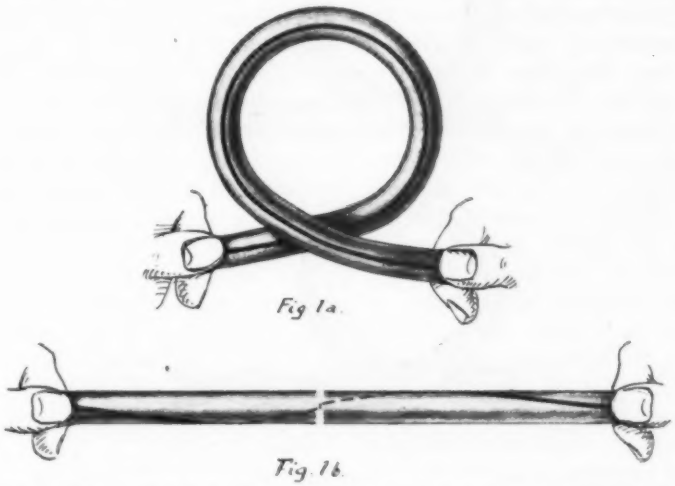

Fig. 1 a and b. The coiled tube is, after drawing out, twisted 360° around its longitudinal axis.

mesenteric axis, and as to the factors active in this case, as well predisposing as causative, I refer to LAURELL's paper of 1926 in this journal and to manuals of surgery.

The axial torsion of the intestine which arises through 180° volvulus can easily be shown on a rubber tube, equipped on one side with a straight longitudinal coloured stripe in order to make the axial torsion more easily visible. Figures 1 and 2 illustrate a volvulus position of such a tube. If the tube is coiled one round, as shown by fig. 1 a, and its extremities are steadily seized and drawn apart without being allowed to rotate, the result, as in fig. 1 b, will be a torsion of 360°. In order that the coiled tube, as shown by the figure, (seemingly in volvulus position) shall become straight and axially untwisted after the drawing out of the tube, its one end must first be twisted once around its longitudinal axis, in the given instance through a supination movement of the fixing

right hand, as fig. 2 a and b show. In fig. 2 a the last-named torsion is spread over a great part of the tube and does not cause any narrowing of its lumen, in fig. 2 b on the other hand it is concentrated upon a short part of the tube, whereby the lumen is strongly narrowed. A similar torsion of the tube as in figures 2 a and b is of course also obtained,

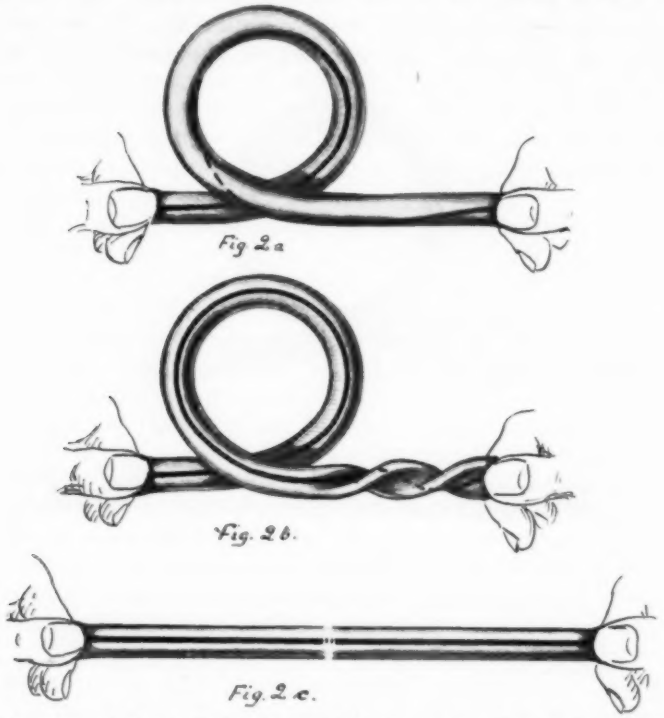

Fig. 2. That part of the coiled tube, which comes from the right, is twisted 360° around its own longitudinal axis through a supination movement of the fixing hand. a) This torsion is spread over a great part of the tube. b) concentrated to a short part of it, whereby its lumen is narrowed, c) the tube, drawn out with fixed extremities, is straight and untwisted. The figure corresponds to a volvulus of 180°.

if the straight, untwisted tube, after that its extremities have been fixed, is twisted as in 180° volvulus. If now the end points of the tube are drawn apart, the longitudinal stripe will run straight as on fig. 2 c, showing that *the spiral course of the tube has completely compensated the axial torsion.*

The experiment illustrated in figures 2 a and b corresponds to a volvulus of 180° of the colon. Either it concerns the sigmoid flexure

or the transverse colon, the colon loop on both sides is more or less steadily attached to the posterior abdominal wall without great possibility to be axially twisted in these places. As, however, a free colon loop which, in normal position, is not axially twisted becomes for some reason twisted 180° around its mesenteric axis and thus lies in a coil, this coil, (which according to figures 1 a and b is corresponded by an axial torsion of 360° of the intestine) must be compensated by an axial torsion as great as the spiral course of the loop but turned in the opposite direction to this coil, (as in figures 2 a and b). It is this axial torsion, which under certain conditions may bring on an obstruction of the intestinal passage, and which may then be radiologically observed. This last-named axial torsion lies chiefly on the free, with mesentery equipped, part of the intestine, for retro-peritoneally attached parts can of course be but inconsiderably axially twisted. The torsion may be situated on both halves of the loop or only on one of them; it may further lie either completely or partly within the twisted loop or completely outside of it. It may be spread over a great part of the intestine, whereby it does not cause a disturbance of the passage and is not visible on roentgen examination, or concentrated chiefly or almost exclusively to a short part of the intestine, whereby a passage obstruction may be the consequence, especially if a great part of the axial torsion, or all of it, is situated on one side of the vertex of the loop or compressed on a short intestinal portion.

The axial torsion of the intestine through volvulus appears on roentgen pictures only if it is concentrated to a sufficiently short stretch of the intestine; it then often appears in the form of an obstructed part with crosswise or spirally arranged opaque stripes, thus impeding the passage of the opaque enema. The crosswise arranged opaque stripes are probably signs of an arrangement of the intestinal mucous membrane in coiled, high folds on the axially twisted part of the intestine. According to FORSSELL it is not a passive folding of the mucous membrane but an active transformation in order to facilitate the passage. Probably the torsion of the muscular layers is the chief cause of the stenosis.

Localized axial torsion of the character described above has been observed in the Roentgen Department, Upsala, in a case of volvulus of the transverse colon[1] and in a series of cases of volvulus of the sigmoid flexure. In all the cases the volvulus has amounted to about 180°. Theoretically, the axial torsion could here amount to 360°, even if it were concentrated to a short part of the intestine. In practice, however, it will only approach this value, as a certain torsion can take place also on that part of the intestine which is retro-peritoneally fixed and on the

[1] This case will be more exhaustively described in a coming paper on »Volvulus of the transverse colon».

volvulus loop itself. In connection with the casuistics I shall later on discuss possible causes of the fact that the axial torsion is concentrated to certain, apparently typical places.

Casuistics

A. Own cases

Case 1. Volvulus of the transverse colon. Surg. Clin. 1260/1933. Picture nr. S. C. 4983. S. D. 9174.

Woman, 69 years. Admitted to the Surgical Clinic (Professor NYSTRÖM) on May 24th, 1933. Suspicion of cancer of the colon. A constipation history of 10 years with increased troubles during the last two months, when also some distention and pains in the upper part of the abdomen have set in. At the admission the general condition was good. *Abdomen: somewhat meteoristic, everywhere soft.* Slight tenderness in the upper part of the abdomen, especially in the hypochondria and in the left iliac fossa.

Roentgen examination May 26th — 31st, 1933.

On opaque enema the sigmoid colon, the descending colon and the left part of the transverse colon were filled without difficulty. Some-

Fig. 3. Volvulus of the transverse colon. (180°.) Standing position after opaque enema.

what to the right of the median line the opaque substance in the transverse colon had the shape of a funnel and here was an obvious obstruction to the passage. The obstruction could only be overcome with difficulty, and part of the enema entered the ascending colon and the caecum.

Roentgenograms now showed volvulus on the left part of the transverse colon, amounting to 180° with the efferent loop half lying ventrally (Fig. 3.) The narrow place was situated somewhat *orally of the crossing-point of the loop halves* and just to the right of the spinal column. Special pictures of this region (Fig. 5) showed barium stripes running crosswise, indicating an axial torsion of the transverse colon. The spiral folds can be followed on the roentgenograms almost one round on a stretch of about 6 cm. When the patient had discharged the enema the transverse colon was contracted and shortened and the volvulus was restored. (Fig. 4.) The previously observed abnormal configuration of the mucous membrane could not now be seen. On an examination made a few days later *there existed again a volvulus* with the same findings as have been described above.

The volvulus of only 180° of the transverse colon, stated on two occasions of examination, seems to be a satisfactory explanation of the troubles of the patient, for it brought on, at least at intervals, a pronounced obstruction of the colonic lumen in *one* place, (not in two places as in common volvulus of about 360°).

Case 2. Volvulus of the sigmoid flexure. Rad. Dep. 3457/1931. Picture nr. S. D. 2787.

Man, 68 years who has been troubled by an obstinate constipation, meteorism, qualms, lack of appetite but no pains, was ambulatory examined. Clinical suspicion of malign tumour.

Roentgen examination April 14th, 1931.

The opaque enema showed a long sigmoid flexure which lay twisted 180° with the afferent half of the loop situated ventrally. Within the volvulus loop on its afferent half, *aborally of the crossing* point, was a relative obstruction to the passage (on the roentgenogram about 2 cm. long), and on this point the opaque stripes were seen running crosswise. (Fig. 6.) The spiral folds can be followed on the roentgenogram not quite one round. No signs of malign tumour within the colon.

The symptoms of the patient were considered to be satisfactorily explained by the observed passage obstruction, which had arisen through the concentration of a great part of the axial torsion to a short part of the intestine.

Case 3. Volvulus of the sigmoid flexure. Surg. Clin. 2294/1933. Picture nr. S. D. 9999.

Woman of 61. 1920 resection of the splenic flexure of the colon, of the descending colon and part of a redundant sigmoid flexure with anastomosis side-to-side, in Sabbatsberg's hospital, Stockholm (Professor NYSTRÖM). After the operation the intestine behaved satisfactorily with laxatives. In the beginning of 1933 appeared troubles in

volvulus loop itself. In connection with the casuistics I shall later on discuss possible causes of the fact that the axial torsion is concentrated to certain, apparently typical places.

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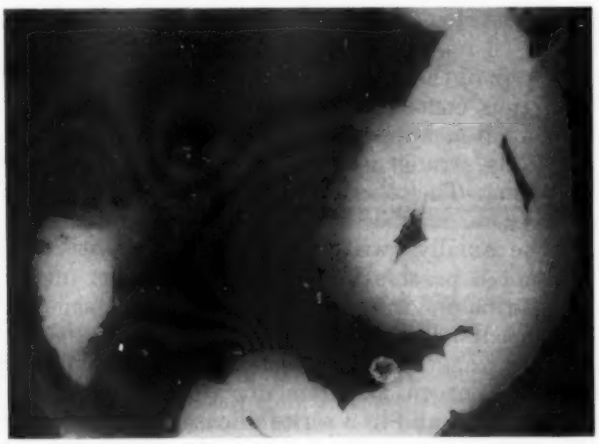

Fig. 3. Volvulus of the transverse colon. (180°.) Standing position after opaque enema.

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the form of constipation, meteorism, pains, during the last time also diarrhoea and rectal haemorrhages. The troubles increased and the patient was admitted to the Surgical Clinic, Upsala. (Professor NYSTRÖM) on Sept. 27th, 1933. The general condition was good. On clinical examination the patient presented *a moderate distension and a limited tenderness in the left iliac fossa*, where plastic resistances, probably scybala, could be palpated.

Roentgen examination Sept. 29th—Oct. 10th, 1933.

Opaque enema showed a rather long, not distended sigmoid flexure which lay down in the pelvis and was twisted in a volvulus of 180°. A mucous membrane relief indicating an axial torsion (crossing opaque stripes) was seen somewhat *orally of the crossing point of the loop halves* and on this place just aborally of the previously made anastomosis it was a relativ obstacle for the enema. The tenderness was also localized to this place. The spiral folds can be traced on the picture for a stretch of about 6 cm. for almost one round. (Fig. 7.) The palpated scybala lumps lay just at the site of the anastomosis, just orally of the stenosis. On reiterated examinations almost identical findings were made, and also after discharge of the opaque enema spiral folds appeared on the roentgenograms but this time over a long stretch of the intestine, showing that the axial torsion was spread over a long distance.

The troubles seem to be satisfactorily explained by an obstructed passage, due to a short axial torsion of the colon in conjunction with accumulation of solid scybala on the oral side of the obstruction. Possibly a local disturbance of circulation or a lesion on the mucous membrane, caused by the solid scybala balls above the axial torsion, can have brought on an intermittent rectal haemorrhage.

Case 4. Volvulus of the sigmoid flexure. Surg. Clin. 5/1932. Picture nr. 1990.

A 51-years old woman who had been treated, since Sept. 29th, 1931, on the Surgical Clinic, Upsala, (Professor NYSTRÖM) for septic coxitis + vitium cordis, was troubled first for some days by meteorism, pains in the abdomen and qualms, and then suddenly got an attack of strongly pronounced distension which were not improved by rectal enemas. The abdomen was very distended and in the left iliac fossa an increased peristalsis was observed.

Roentgen examination Febr. 11th. 1932.

Survey roentgenograms of the abdomen, showed that the whole of the colon was strongly distended by gases and liquid contents; especially imposing was an enormous colon loop in the right flank. The barium enema met with an obstruction in the sigmoid not far from the rectum. The stenosis was a few cm. long and could be passed by a small amount of opaque substance. Volvulus of probably about 180° appeared to be present. The constricted place showed spiral folds of the mucosa. The

axial torsion within the constricted part seemed to correspond to almost one turning and was situated on the efferent loop half at the crossing point of the loop halves. (Fig. 8.)

On the return from the roentgen examination to the Surgical Clinic the patient discharged the enema, and also large quantities of flatus were passed. The troubles then disappeared.

The case is an instance of an acute attack of volvulus, where obstruction of the passage was localized to the efferent loop half and was due to an axial torsion. The strongly pronounced meteorism may be regarded as an argument for the supposition that there has also existed a disturbed circulation from some cause besides the passage obstruction. Possibly there was a general cardiac insufficiency, or a local strangulation of the vessels.

B. Previously radiologically observed cases of axial torsion of the large intestine in volvulus

In the literature accessible, relative stenosis with crosswise arranged mucous folds of the mucosa or axial intestinal torsion in volvulus has only exceptionally been described; and then the mechanism of the genesis has not been more closely discussed. Concerning the colon, BERG seems first to have made such an observation in a case of volvulus of 180° of the sigmoid flexure and he has published a beautiful picture of it in 1932.

The case was a 28-years old woman who had had, for one year and a half, gradually increasing abdominal troubles which had become accentuated to violent attacks of pain with limited tenderness in the left lower part of the abdomen. The roentgen picture published shows an uncommon form of about 180° volvulus on the sigmoid flexure which lay twisted laterally downwards to the left. Within the twisted loop of the intestine on a short part spiral opaque stripes appear which can be followed almost one round. Here an obstruction of the intestinal passage existed, and BERG characterizes this place as the fixed torsion point. On operation (Professor NORDMANN, Berlin) a strong shrinking of the mesentery was found in this place, (between the oral part of the sigmoid and the posterior abdominal wall). The crossing point of the loop halves, in other words the twisting point of the sigmoid loop, is situated on the roentgen picture somewhat orally of this constricted place. Thus, according to my opinion, it is here the question of an axial, about 360°, torsion by 180° volvulus. After the discharge of the enema the long sigmoid flexure collapsed to an inconsiderable size and became displaced to the right, whereby the volvulus was untwisted and the spiral folds disappeared.

LIGAT and OVEREND have made similar observations in two cases of volvolus of the sigmoid flexure and give a picture of one of them in 1933.

This case was a 26-years old woman who had suffered, since one year, from periodical attacks of severe abdominal pain with distension, severe constipation, tenderness in both iliac fossae. Roentgen examination showed a long sigmoid flexure. On the picture published the sigmoid flexure seems to be twisted about 180°, and somewhat orally of the crossing point of the loop parts is seen an axial torsion with spiral mucous folds. These run over a relatively long intestinal section and there does not seem to have existed any obstacle for the enema although the lumen seems to be somewhat narrowed.

LÖW-BEER has observed a corresponding picture in a case of volvulus of the ventricle. According to LIGAT and OVEREND spiral mucous folds are a direct sign of volvulus, equivalent to loop halves twisted around each other. As far as I can see this symptom is in itself not proof of a volvulus. Spiral folds can namely also arise by axial torsion of the intestine without a volvulus being at hand. Thus, for instance RIEDEL describes two cases of axial torsion of the transverse colon by dislocation and fixation through adhesions upwards backwards of the great omentum and pulling on its colon insertion. Principally corresponding observations have been made by AIGROT concerning the sigmoid colon.[1]

Thus, to be sure of the diagnosis »volvulus», we can not exclusively rely on an observed axial torsion or a torsion-like picture on a limited intestinal portion, but we must first make certain that there is a twisting of the intestinal loop around its mesenteric axis which will, as a rule, be possible. The axial torsion arising in volvulus, is, on the other hand, of great theoretical interest, as it can in certain cases, explain the origin of a pronounced enteric obstruction already by a volvulus of 180°, in itself physiological. Also a local disturbance of the circulation may arise through the compression of a few veins in the mesentery of the axially twisted part of the intestine, a circumstance, which has possibly contributed to the rectal haemorrhages in case 3.

If we compare the localization of the axial torsion in my cases, and in those published in the literature, with the crossing points of the loop halves, we find that the torsion is localized, sometimes just at this latter point (Case 4), sometimes a little bit laterally and then either within the twisted intestinal loop, viz. the ventricle (Case 2, BERG's case of volvulus of the sigmoid flexure, and LÖW-BEER's of volvulus of the ventricle)

[1] These observations are made at laparotomies.

or outside and orally of the volvulus loop (Cases 1, 3 and the case of LIGAT's and OVEREND's). The axial torsion can also be thought concentrated to the efferent loop half and aborally of the crossing point of the loop halves, but I have not observed any such case. This variable position of the axial torsion in these cases of a slight volvulus of 180° talks in favour of the supposition that the crossing point of the loop halves does not play any essential part for the position of the axial torsion. The latter seems, on the other hand, in all the cases to be connected with places, where the free mesentary begins or ends. The right colon flexure is, as is well known, directly attached to the posterior abdominal wall, the parietal peritoneum from the anterior surface of the right kidney going, under normal conditions, directly over to the superior anterior wall of the colon on the right side. The transverse mesocolon begins in the vicinity of the head of the pancreas, (CORNING, SPALTERHOLTZ), and it is in this region that was situated the visible axial torsion in case 1 (volvulus of the transverse colon). In one of the cases of volvulus of the sigmoid flexure it was situated, according to the same rule, near the rectum and in the other cases in the left iliac fossa in the region where a free mesosigmoid generally begins. This could also be proved on operation in BERG's case. In these places the more or less fixed attachment of the intestine to the posterior abdominal wall forms a certain obstacle for a further progression of the axial torsion on retro-peritoneally fixed intestinal parts. Essentially the same condition existed in LÖW-BEER's case of volvulus of the ventricle in which the spiral folds were situated on the intra-abdominal part of the oesophagus.

Thus, if we may presume, in volvulus up to 180°, that a concentration of the axial torsion on a short intestinal portion can give rise to a stenosis, there remains to seek for the causes of this concentration. Such a cause, and perhaps the most important one, is obviously connected with the distension of the twisted loop. For if a colon loop, twisted 180° around its mesenteric axis is rather empty and collapsed, the axial torsion is generally extended over a large part and then it does not bring on any obstruction of the intestinal passage. We have then a *genuine physiological volvulus* of 180°. But if the loop is filled with large quantities of faeces or flatus, the volvulus loop will try, first of all, to be spontaneously restored and secondly, if lack of space in the abdomen prevents such a spontaneous reposition, to be axially untwisted in a maintained volvulus position in accordance with Fig. 2, because the elastic forces, which appear in the intestinal wall on its distension, strive to give back to the intestine its normal anatomical untwisted appearance. By this, on increasing intestinal content, the compensatory axial torsion (Fig. 2) will become displaced outside the volvulus ring, either along both the loop halves or only one of them, as in the cases described above, and so

far that the fixation of the intestine directly to the posterior abdominal wall prevents a further progression of the axial torsion; the torsion will therefore be concentrated towards this point. If the loop is distended still more, the diameter of the ring or rather the coil will increase whereby the afferent and efferent halves of the loop are displaced in relation to each others. Such an increase of the volvulus loop can of course also take place at an earlier stage, simultaneously with the wandering of the axial torsion. The length of the mesentery will finally be deciding for the position of the crossing point in relation to the local axial torsion. If the mesentery of one of the loop parts is comparatively long, this part can be displaced past the narrowed place as in case 2 and in BERG's case, and this loop half (the efferent one in the above-mentioned cases), will then cross the other one (the afferent gut), orally of the stricture. In a volvulus of 360° or more the crossing point of the loop parts will coincide as a rule, as is well known, with the axial torsion points, which are two in these cases (TREVES, MC IVER), and which lie as close to the mesenteric extremities as possible.

GILBERT and KADRNKA have recently emphasized that a retraction of the mesentery can give rise to a configuration of spiral folds on the roentgen picture and in accordance with this opinion they have interpreted the picture published by BERG. Refering to the analysis above, I am not able to join the opinion of GILBERT and KADRNKA. According to my opinion the mesentery by volvulus of 180° does not, as a rule, play any rôle for the appearance of the spiral folds, even if it can not be denied that a local shrinking of the mesentery may sometimes cause pictures, similar to those by genuine torsion.

It is a noteworthy circumstance that the constricted place, in the majority of cases observed, has been situated on the afferent loop half,

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Plate I.

Fig. 5. Volvulus of 180° of the transverse colon. Detail roentgenogram which shows a concentrated axial torsion with stenosis of the passage and spiral folds of the mucosa about one round, orally of the volvulus loop. (Same case as on Fig. 3.)

Fig. 6. Volvulus of 180° of the sigmoid flexure. Concentrated axial torsion with passage obstruction and spiral folds of the mucosa, almost one round within the volvulus loop to the right of the crossing point of the loop parts.

Plate II.

Fig. 7. Volvulus of 180° of the sigmoid flexure. Detail roentgenogram showing a concentrated axial torsion with passage obstruction and orally of the volvulus loop spiral folds of the mucosa, which can be traced about one round. The intestinal blind pocket to the right (X), belongs to the anastomosed colon.

Fig. 8. Volvulus of 180° of the sigmoid flexure. Detail roentgenogram showing concentrated axial torsion with passage obstruction and spiral folds of the mucosa (almost one round) at the crossing point of the loop parts.

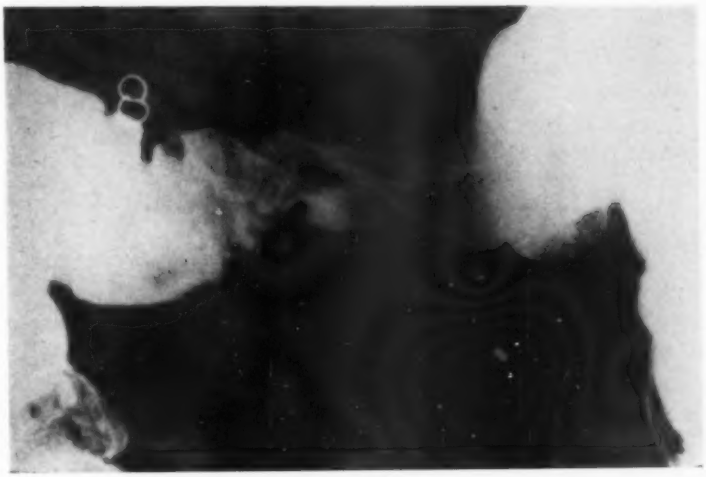

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

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and the question arises, if the enema could have caused this position. This is naturally possible, but on the other hand it is not necessarily so. This is illustrated by Case 3. Here the spiral folds on the whole retained their position on the afferent loop half, even after discharge of the enema, i. e. when the fluid had flowed through the axially twisted place isoperistaltically. Also in LÖW-BEER's case of volvulus of the ventricle the axial torsion lay orally. Apparently it is chiefly the elastic forces of the intestinal wall which displace the torsion, not the movement of the intestinal content.

On spontaneous reposition of the volvulus.

A few words may here be added on the spontaneous, viz. not operative detorsion of volvulus. Spontaneous reposition of a volvulus of the sigmoid flexure was earlier considered to occur only in rare cases, possibly in conjunction with rectal enemata. LAURELL and others have emphasized, however, that spontaneous reposition is a common occurrence in volvulus. Concerning the volvulus of the flexure nowadays a sigmoid colon with the loop halves lying close to each other is regarded as an indirect sign of a passed volvulus, if the clinical picture admits the supposition of such a disease, and such cases are also treated as volvulus (FERNSTRÖM, LIGAT and OVEREND). As LAURELL has proved, a detorsion of the volvulus loop may take place in essentially the same way as the twisting starts, provided that the loop is not so distended that the space in the abdomen prevents a detorsion. By appropriate twisting of the body the two loop halves, if they have a different specific gravity, can glide against each other, as the specifically heavier intestinal part strives to place itself lowest in the abdomen. As STENBERG, EDGREN, BLOODGOOD and others have shown, a detorsion may take place also if it is possible to empty the twisted loop through the insertion of an intestinal tube into the efferent half, passing the occlusion.

Fig. 4. Same case as on fig. 3 after discharge of the enema. The transverse colon contracted and shortened. The volvulus is replaced.

Another mechanism of reposition existed in Case 1 and probably also in Case 4. Immediately as the patient discharged the enema and the transverse colon was contracted and shortened, the volvulus was restored. (Fig. 3 before and Fig. 4 after discharge of the enema.) The intestine thus reacted essentially in accordance with the experiment with the rubber tube which has been described on page 4. When the extremities of the twisted loop were drawn apart the »volvulus» disappeared. A similar mechanism seems probable in BERG's case too, where the volvulus was spontaneously untwisted after the discharge of the enema.

Along with the previously described mechanisms of detorsion which have concerned common volvulus with a twisting of more than 180°, I should want to emphasize the fact that reposition of volvulus may arise through a contraction of the intestine and a consecutive shortening. Such a mechanism can of course arise more easily in those cases of slight volvulus with free passage for the intestinal contents, in one direction or the other or in both, which are described in this paper, than in a pronounced pathological volvulus. In these latter cases, especially those which come to operation and have the loop halves or their foot points fixed close to each other through shrinking processes of the mesentery, this mechanism will only play an unimportant part. It does not seem improbable to me that the replacing effect which a rectal enema may have on a volvulus (of which several observations described in the literature, besides cases 1 and 4, give evidence), can be explained by the contraction and subsequent shortening at the discharge of the enema. The effect of an inserted intestinal tube is apparently also important. In certain cases it made the evacuation of the intestine possible.

SUMMARY

The so-called physiological volvulus of 180° may also give rise to a tempory obstruction of the enteric tube and possibly also to a localized disturbance of the circulation. This depends upon the axial torsion of the loop halves always accompanying a volvulus position. The stenosis arises from the circumstantial concentration of this axial torsion on a localized stretch of the gut. On the other hand the obstruction may be relieved if the torsion against spreads over a greater part of the intestine or if the volvulus becomes untwisted. These processes are illustrated by cases of volvulus of 180° situated on the transverse colon or sigmoid flexure. On the roentgenogram a localized axial torsion appears at spiral stripes of the opaque matter in a stenosed part of the colon. The localized axial torsion is to be found where the mesentery of the twisted loop begins or ends. Its position on the loop is independent of the situation of the crossing point of the two loophalves. Thus it may either coincide with or lie laterally of this latter point on the volvulus loop or outside of it. The most important cause of this concentration of the axial torsion and the consecutive stenosis seems to be the distension of the volvulus loop. A physiological volvulus of 180° may be restored by contraction and the ensuing shortening of the gut.

ZUSAMMENFASSUNG

Auch bei einem sogen. physiologischen Volvulus von 180° kann ein vorübergehendes Hindernis für die Darmpassage entstehen, und vielleicht auch ein lokalisiertes Zirkulationshindernis dadurch, dass eine Volvuluslage der Darmschlinge immer von einer axialen Torsion der Schlingenschenkel begleitet ist, und dass diese axiale Torsion unter gewissen Umständen auf eine kurze Strecke des Darmes zusammengedrängt sein kann, wobei dieser stenosiert wird. Umgekehrt kann ein solches Torsionshindernis behoben werden, wenn die Torsion sich wiederum über einen längeren Darmabschnitt verteilt, oder wenn eine Reponierung des Volvulus eintritt. Diese Verhältnisse illustriert Verf. durch Mitteilung von Fällen eines Volvulus von ca. 180° am Colon transversum, bezw. solchen am Colon sigmoideum. Auf der Röntgenplatte äussert sich eine lokalisierte axiale Torsion in Form von spiralförmig verlaufenden Kontraststreifen im Zusammenhang mit einer Verengung des Lumens. Die lokalisierte axiale Torsion ist dort zu suchen, wo das Mesenterium der umgedrehten Schlinge beginnt oder aufhört; ihre Lage am Darm ist unabhängig von der Kreuzungsstelle der Schlingenschenkel, indem die Torsion mit dieser zusammenfallen oder neben der Kreuzungsstelle liegen kann, entweder in der umgedrehten Schlinge oder ausserhalb von ihr. Die wichtigste Ursache der Lokalisierung der axialen Torsion und des dadurch entstehenden Passagehindernisses dürfte die Ausdehnung der Volvulusschlinge sein. Bei physiologischem Volvulus von 180° kann Reponierung des Volvulus auch durch Kontraktion und dabei entstehende Verkürzung der Darmschlinge zustandekommen.

RÉSUMÉ

Il peut survenir, même dans les volvulus à 180° dits physiologiques, un obstacle à la perméabilité intestinale et peut-être aussi une entrave circulatoire localisée, du fait qu'une torsion axiale des extrémités de l'anse accompagne toujours la position en volvulus de l'anse intestinale, et que cette torsion axiale peut, dans certaines conditions, se concentrer à une courte partie de l'intestin, déterminant une sténose. Inversement cet obstacle par torsion peut disparaître si la torsion se répartit sur une plus grande section d'intestin ou par réduction du volvulus. Ces particularités sont illustrées par un cas de volvulus à environ 180°, siégeant sur le colon transverse et par quelques cas pareils sur l'anse sigmoïde. A la radiographie, une torsion axiale localisée se traduit par une traînée de contrast en spirale coïncidant avec une sténose de la lumière. La torsion axiale localisée doit être cherchée au point où commence ou finit le mésentère de l'anse tordue; son siège est indépendant du point de croisement des extrémités de l'anse, en ce sens que la torsion peut coïncider avec ce point de croisement ou se trouver sur le côté de ce point, soit en dedans, soit en dehors de l'anse tordue. La cause principale de cette localisation de la torsion axiale et de la sténose qui en résulta réside sans doute dans la distension de l'anse du volvulus. Dans le volvulus physiologique, la réduction de ce volvulus peut également se faire par contraction et raccourcissement consécutif de l'anse intestinale.

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DIE PORZELLANGALLENBLASE IM ROENTGENBILD[1]

(Bericht über zwei Fälle)

von

Roland Blatter

(Tabula XXXI)

Obwohl eine Verkalkung der Gallenblasenwand für den Anatomen durchaus keinen seltenen Befund darstellt, und der Pathologe ab und zu, nach EWALD häufiger als die Chirurgen glauben, Gelegenheit hat, diese eigenartige Veränderung als Zufallsbefund auf dem Sektionstisch zu beobachten, sind doch die Angaben darüber in Lehr- und Handbüchern äusserst spärlich.

So erwähnt ASCHOFF, dass die Verkalkung der Gallenblasenwand ein seltener Befund sei. Sie könne über die ganze Blase ausgebreitet sein und manchmal alle Wandschichten durchsetzen, sodass die Gallenblase dann ein hartes schalenartiges Gebilde darstellt. KAUFMANN vergleicht die durch eine diffuse Fibrose veränderte, dicke, schwielige, aussen oft ganz glatte Gallenblasenwand, die auch verkalken, teilweise sogar verknöchern kann, mit einer arteriosklerotisch veränderten Gefässwand. Er betrachtet diesen Vorgang, in ähnlicher Weise wie SCHMAUS, als Abschluss einer chronisch produktiven, fibroplastischen Entzündung der Gallenblase. Es kann aber auch in seltenen Fällen die phlegmonös-eitrige und nekrotisierende Form der Entzündung zu einer mehr oder weniger vollständigen Petrifikation der Wand führen, wenn in das phlegmonöse Exsudat der Wandabszesse eine Kalkablagerung stattfindet und keine Fortschaffung durch Resorption oder Durchbruch erfolgt. Diese Verkalkungen können schliesslich auch das neugebildete hyalinisierte Narbengewebe der Wand betreffen und dieselbe in einen starren Panzer umwandeln. (ASCHOFF und BACMEISTER, HENKE und LUBARSCH.)

Gegenüber der Theorie, welche mehr entzündliche Veränderungen innerhalb der Wandung für den Verkalkungsprozess verantwortlich macht, steht die Hypothese der Autoren, die eher mechanische Vorgänge als Ursache der Verkalkung ansehen.

So glaubt FLÖRCKEN, eine Hydropisierung der Gallenblase infolge des Cysticusverschlusses verantwortlich machen zu dürfen. Der Druck, der durch den Blaseninhalt ausgeübt wird, verursacht in der Wandung eine fortschreitende Degeneration. Das gesunde Gewebe wird durch ein fibröses Narbengewebe ersetzt, das schliesslich verkalken kann, wobei vielleicht infolge von Stoffwechselstörungen eine Kalkresorption aus dem Galleninhalt erfolgt. Als Grundlage der Verkalkung hält er als sehr wahrscheinlich die mangelhafte Blutversorgung des Organs, die eventuell durch eine isolierte Sklerose der

[1] Bei der Redaktion am 27. I. 1934 eingegangen.

A. cystica bedingt ist. Da bei seiner Beobachtung entzündliche Momente sowohl klinisch als auch histologisch fehlen, bezeichnet er das Leiden Cholecystopathia chronica calcarea. In ähnlicher Weise äussern sich PHEMISTER, REWBRIDGE und RUDISILL.

Es lassen sich vom pathologisch-anatomischen Standpunkt aus zwei Typen der Verkalkung der Gallenblasenwand unterscheiden: nämlich die kleine geschrumpfte Form und die grosse hydropisch erweiterte Form, die bis Kindskopfgrösse erreichen kann (Fall KOENIG). Beide Arten sind entweder frei beweglich, oder durch entzündliche Adhärenzen mit den Nachbarorganen verwachsen. Die Inkrustation ist entweder generalisiert oder zirkumskript, inselförmig. Der Blasenhals bleibt meist frei von Petrifikation.

Ebenso spärlich, wie die pathologisch-anatomischen Angaben, finden sich Beobachtungen von röntgenologischer Seite. Ich erwähne die Arbeiten von BAYLESS und SKINNER, CHIRAY und PAVEL, DIENSTFERTIG, FLÖRCKEN, FOWLER, GOLDHAMER, HAENISCH, HERZ, KOENIG, PHEMISTER, ROBB, SESSA, SUTHERLAND, TALBOT. In seiner »Röntgendiagnostik des Verdauungskanals» bezeichnet ALBRECHT die »Porzellangallenblase» als seltene Beobachtung. Typische Röntgenbilder von drei Fällen von verkalkter Gallenblasenwandung finden sich bei EISLER und KOPSTEIN.

Zu diesen wenigen röntgenologischen Beobachtungen können nun durch vorliegende Arbeit zwei weitere in ihrer Art äusserst charakteristische Fälle der durch FLÖRCKEN als »Porzellangallenblase» bezeichneten Wandverkalkung hinzugefügt werden.

Im *ersten Fall* handelt es sich um eine 36 jährige Patientin mit folgender Anamnese:

»Seit vielen Jahren ausgesprochene Magenbeschwerden, was Patientin mit ihrem Berufe (Schneiderin) in Zusammenhang bringt. Patientin war immer obstipiert, hatte wenig Appetit, mochte sonderlich keine fetten und schweren Speisen geniessen. Häufige Anfälle von Übelkeit, Schmerzen im Oberbauch, Brechreiz, oft Erbrechen von Schleim. Bei schweren Anfällen erbrach Patientin Galle, anschliessende Schmerzen in der Lebergegend. Es traten auch ikterische Verfärbungen um die Augen auf, nie ausgesprochener Ikterus. Anfälle gingen stets auf Diät und Bettruhe zurück. 1930 im Anschluss an besonders starken Anfall der erwähnten Magenbeschwerden treten Symptome einer Appendicitis auf, starkes Stechen im rechten Unterbauch, Erbrechen. Diese Anfälle treten immer wieder bei Vernachlässigung der dauernd geübten Diät auf. Letzter Anfall im Mai 1932. Patientin tritt am 8. 9. 32. in die chir. Klinik ein, um sich appendektomieren zu lassen.»

Aus dem Status praesens: »mittelgrosse Patientin in gutem Ernährungszustand. Abdomen weich, nicht schmerzhaft. Keine Défense. Leichter Druckschmerz am Mac Burney'schen Punkt. Kein Entlastungsschmerz, kein Fernschmerz.»

Während nun die klinische Untersuchung vollständig normale Verhältnisse, keinen Palpationsbefund ergibt, wird durch die *Röntgenuntersuchung* sogleich die Gallenblase als Urheberin des Krankheitszustandes erkannt. Sie zeichnet sich auf der ganzen Aufnahmeserie als birnförmiger, scharfkonturierter, inhomogener Schatten ab mit scheckiger, unregelmässig fleckiger Struktur. Der Rand ist entsprechend der unregelmässigen

Kalkeinlagerung in vielen unzusammenhängenden Platten stellenweise unterbrochen. Auf einer Liegendaufnahme ist eine deutliche Impression des Bulbus duodeni bemerkbar. Besonders schön präsentiert sich der Schatten auf einer gezielten Aufnahme. (Abb. 1.) Der Stand der Blasenkuppe variiert je nach der Lage (liegend, stehend) zwischen der Höhe des zweiten und vierten Lendenwirbels. Auf Grund dieser Bilder wurde durch den Röntgenologen Herrn Prof. LÜDIN die Diagnose Porzellangallenblase gestellt. Sie wurde in vollem Masse bestätigt durch die vorgenommene Operation, die ein typisches Exemplar einer verkalkten Gallenblase zu Tage förderte.

Abb. 2. Patholog. anatom. Preparat von Fall 1 (Abb. 1)

Operationsbefund (chir. Klinik der Universität Basel. Prof. HENSCHEN): »Magen normal, ohne ulcusverdächtigen Befund. Sofort präsentiert sich die stark vergrösserte, prall gefüllte Gallenblase mit verdickter Wandung, die nicht akut entzündet scheint. Der Cysticus ist posthornförmig doppelt abgebogen, die Wand verdickt, im Cysticus zwei fast kirschgrosse Steine durchtastbar. Punktion der Gallenblase ergibt gelben rahmigen Eiter.«

Das exstirpierte Organ ist stark vergrössert (10 : 4 : 4 cm) und besitzt durchwegs eine vermehrte Wanddicke (3—5 mm). Das ganze Gebilde ist vollständig starr, sodass nach Entleerung des rötlichbraunen, schmierigen Inhaltes die Wände nicht zusammenfallen. Die Aussenfläche zeigt zahlreiche gestaute Gefässe und vermehrte bindegewebige Auflagerungen, die auf eine durchgemachte Pericholecystitis hinweisen. Auf dem Querschnitt ist die Wand gelblich, zum Teil sieht man hyalines Narbengewebe, zum Teil in Platten angeordnete Kalkeinlagerungen. Hals und Cysticus sind weniger verdickt und nicht verkalkt. Auch in diesem Falle ist der Cysticus durch zwei auf den Röntgenbildern nicht erkennbare Steine verschlossen. Die Innenfläche der Gallenblase besitzt infolge der eingelagerten Kalkplatten eine kleinhöckerige Struktur.

Röntgenaufnahmen des Präparates (Abb. 2) lassen sehr schön die Marmorierung infolge der in Spangen und Platten angeordneten Kalkeinlagerungen erkennen. Der Verkalkungsprozess hat sich hauptsächlich

im Fundus abgespielt, während Blasenhals und Cysticus nur eine diffuse Wandverdickung, keine Kalkschatten mehr zeigen.

Bericht der pathologischen Anstalt der Universität Basel (Prof. GERLACH): »Sehr derbe, starrwandige Gallenblase, die als Inhalt eine rötlichbraune, schmierige Masse enthält, durchmischt mit kleinen schwärzlichen Konkrementen. Die Innenauskleidung besteht teilweise aus stark verkalkten Platten, die Wandschichten überall deutlich verdickt. An der Aussenfläche sind die Gefässe gestaut, ebenfalls findet sich hier eine vermehrte bindegewebige Auflagerung. Ausführungsgang wenig verkalkt und eingeengt.

Untersuchte Stellen aus dem Fundus und aus dem Halsteil der Blase zeigen, dass sich die Wand meistens aus einem stark verschwielten und deutlich mit Kalk imprägnierten Gewebe aufbaut. Die derben Bindegewebsmassen sind teilweise kernlos, hyalin gequollen. Dazwischen eingelagert finden sich wieder ausgedehnte zellige Infiltrate, hauptsächlich im Verlauf von Gefässen, wo sich gehäuft eosinophile Zellelemente vorfinden. Diese letztere Zellart ist in sämtlichen Schichten in vermehrter Weise eingestreut. Auch kleinzellige Elemente finden sich vermehrt eingelagert. Schleimhautstücke lassen sich histologisch nicht mehr nachweisen, nur hie und da sind noch Reste von Gängen aufzufinden. Der Innenwand aufgelagert finden sich nekrotische Massen und teils grosse Zellelemente, die Fettkörnchen eingelagert haben. Gallepigment findet sich wenig. Hämosiderin ist ebenfalls nur an wenigen Stellen vorhanden. Der Blasenausgang zeigt weniger verödete und mit Kalk beladene Bezirke. Auch die Wandschicht, ebenfalls um das Vielfache verbreitert, zeigt starke hyaline Verödung. Entzündliche Infiltrate finden sich auch reichlich, hauptsächlich im Verlauf der Gefässe. Im Verhältnis zu andern Gallenblasen, die untersucht wurden, zeigt dieser schwere sklerotisierende Zustand eine ganz geringe Pigmentablagerung.

Diagnose: Schwere chronische Cholecystitis mit starker hyaliner Degeneration der Wand und Kalkablagerung. Cholelithiasis.»

Der *zweite Fall* betrifft einen 56 jährigen Dienstmann, der wegen eines inoperablen Pyloruskarzinoms in die chirurgische Klinik aufgenommen wurde. In seiner Anamnese finden sich ausser einem seit wenigen Tagen vor dem Spitaleintritt aufgetretenen Druckgefühl auf dem Magen keinerlei Angaben über Abdominalbeschwerden.

Aus dem Status praesens: »Grosser, schmächtig gebauter Mann in mässig gutem Ernährungszustand. Abdomen: weich. Leberdämpfung zwei Querfinger unter dem Rippenbogen. In der Mammillarlinie rechts eine Vorwölbung nach unten palpabel, von derber Konsistenz, höchstwahrscheinlich Gallenblase. Palpation in der Nierengegend nicht schmerzhaft.»

In diesem Falle fehlen in der Anamnese im Gegensatz zum vorigen jegliche Angaben, die auf ein Gallenblasenleiden deuten würden. Die klinische Untersuchung ergibt einen deutlich palpablen, harten, nicht druckempfindlichen Tumor in der Gallenblasengegend.

Aber auch in diesem Fall wird die Diagnose auf Verkalkung der Gallenblasenwand erst anhand der dafür wiederum sehr charakteristischen *Röntgenbilder* gestellt. Auf allen Aufnahmen gibt sich die Gallenblase deutlich als gänseeigrosser, ovaler, fast homogener Schatten mit scharfer, stellenweise unterbrochener Kontur, zu erkennen (Abb. 3). Er liegt parallel zur Lendenwirbelsäule mit der Kuppe in der Höhe des vierten Lumbalwirbels. Auf einer zweiten Aufnahme ist der Blasenschatten direkt vor

die Lumbalwirbelsäule verlagert (Abb. 4), was auf eine, trotz der enormen Wandverdickung, verwunderlich gute Beweglichkeit deuten und pericholecystitische Verwachsungen ausschliessen lässt.

Operationsbefund (Chir. Klinik. Prof. HOTZ): »Faustgrosses Karzinom am Pylorus, das auf die Gallengänge übergreift. Auf der Leberoberfläche grosse Metastasen. Die Gallenblase ist sehr stark verdickt, steinhart und zirka gänseeigross.»

Die Diagnose auf »Porzellangallenblase» findet ihre Bestätigung durch die Autopsie, die eine stark vergrösserte (9 : 5 : 4 cm), dickwandige (3—4 mm) Gallenblase ergibt. Das Sektionsprotokoll der patholog.-anatomischen Anstalt gibt an: »Gallenwege leicht durchgängig mit Ausnahme des Ductus cysticus, welcher in eine über hühnereigrosse, allseits von einer sehr dicken kalkigen Schale umgebenen Gallenblase mit verschlossenem Ausgang mündet. Im Innern des Gebildes findet sich grauer eingedickter Eiter. »Die Oberfläche dieser Gallenblase ist vollständig glatt und weist keinerlei Zeichen einer durchgemachten Pericholecystitis auf. Die Wand ist gelblich mit viel ausgedehnteren Kalkeinlagerungen als im vorigen Fall. Hier ist auch der Blasenhals vom Petrifikationsprozess betroffen. Die Innenfläche ist ebenfalls kleinhöckerig, schwielig mit erkennbaren, durchscheinenden Kalkplättchen. Im Fundus liegt ein kirschgrosser Stein.

Das *Röntgenbild des Präparates* (Abb. 5) weist ebenfalls eine kleinfleckige, scheckige Schattenbildung auf. Fundus und Blasenhals sind vollständig gleichartig verkalkt. Der im Fundus befindliche Stein ist als diffuse Verschattung erkennbar.

In diesen zwei eben beschriebenen Fällen haben wir typische Vertreter der *»Porzellangallenblase»* vor uns. Eine starrwandige, knochenharte Gallenblase mit beträchtlich vermehrter Wanddicke, die zur Eröffnung die Verwendung einer Säge erfordert und die beim Beklopfen mit einem metallischen Gegenstand einen klingenden Ton ergibt. Die Farbe ist gelblich, und das Organ sieht aus »wie aus Porzellan» (FLÖRCKEN). Der Inhalt ist, wohl infolge des vorhandenen Cysticusverschlusses, nicht mehr richtige Galle, sondern eine weiche, breiige Masse von rötlichbrauner Farbe. Die Innenfläche gleicht ganz einer atheromatösen Aorta. Der Ductus cysticus ist obturiert, wie in den meisten bisher beschriebenen Fällen, wo er entweder durch gewöhnliche Gallensteine oder durch ein fibröses entzündliches Gewebe verschlossen gefunden wurde.

Auch die histologische Untersuchung von Teilen des Gewebes einer solchen verkalkten Gallenblasenwand entspricht genau den von andern Autoren (CHIRAY und PAVEL, DIENSTFERTIG, FLÖRCKEN, GOLDHAMER, PHEMISTER, ROBB) gemachten Beobachtungen: Die verschiedenen Wandschichten der Gallenblase sind nicht mehr zu erkennen. Die Verkalkung betrifft die ehemalige Muscularis und Submucosa. Die Mucosa fehlt oder ist noch in Resten angedeutet. An Stelle der Muscularis findet sich ein derbes, vollkommen kernloses, hyalin degeneriertes Bindegewebe mit reichlich azidophiler Interzellularsubstanz, entsprechend der hyalinen Umwandlung. Besonders intensiv ist die Verkalkung in den tiefen Schichten der Muscularis, wo der Kalk viele kleine und grössere, nicht

zusammenhängende Inseln bildet. Hie und da treffen wir perivasculäre Entzündungsherde und Kapillarproliferationen, die jedoch um so seltener werden, je weiter der Verkalkungsprozess fortgeschritten ist. In solchen Partien fehlen die Gefässe auf weite Strecken. Die Serosa ist an der Umwandlung nicht beteiligt.

Klinisch macht die Porzellangallenblase in den meisten Fällen keinerlei Beschwerden. Anamnestische Angaben, die auf ein Gallenblasenleiden hinweisen, wie im ersten beschriebenen Fall, sind selten. Ikterus wurde nie beobachtet. Oft handelt es sich, wie bei der zweiten Beobachtung, um einen Nebenbefund bei Krebsen des Magendarmtraktus, der Gallenwege oder der Leber, oder um einen Autopsiebefund bei alten Leuten. Nach CHIRAY und PAVEL war das Alter in 14 von 20 Fällen über 70 Jahre. Frauen sind häufiger befallen als Männer (15 : 5).

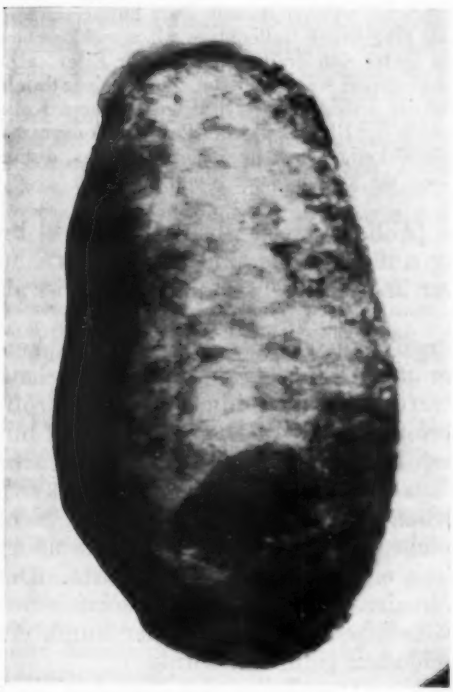

Abb. 5. Patholog. anatom. Preparat von Fall 2 (Abb. 3 und 4).

Die Diagnose stützt sich wegen des Mangels an klinischen Symptomen ausschliesslich auf den Palpationsbefund und auf die Radiographie. Der Tastbefund ist inkonstant je nach der Grösse der verkalkten Gallenblase und der Adipositas der Bauchdecken. In den Fällen, wo ein Tumor palpabel ist, findet er sich in der rechten Mammillarlinie einige Querfinger unterhalb des Rippenbogens, verschieden tief, nicht druckempfindlich und von ausserordentlich derber, harter Konsistenz.

Dem gegenüber steht die grosse Sicherheit, ja Untrüglichkeit der Röntgendiagnose. Nach HAENISCH herrscht zur Zeit die Ansicht vor, dass der ohne Cholecystographie sichtbare Gallenblasenschatten einer pathologischen Gallenblase entspricht, sei es nun, dass die Schattenbildung infolge verdickter Wandung oder durch Kalkinkrustation bedingt ist. Wie bei den bisher publizierten Aufnahmen von Porzellangallenblasen finden wir diese auch in unsern beiden Fällen sehr deutlich sichtbar als

scharfkonturierten, intensiven, ovalen oder birnförmigen Schatten mit einer, durch die verschiedenen Verkalkungsgrade bedingten kleinfleckigen Struktur. Die Lage des Schattens ist entsprechend der Variabilität der Lage des Organs in weitem Masse verschieden, wie auch der an zweiter Stelle beschriebene Fall deutlich zeigt. Meist liegt der Schatten in dem Winkel zwischen rechter 12. Rippe und Lendenwirbelsäule, parallel zu dieser. In der Regel schneidet der untere Pol mit dem zweiten Lendenwirbel ab, doch kann die stark vergrösserte Gallenblase bis weit unter die Crista iliaca herunter reichen. Da je nach der Richtung der Blasenachse zum Zentralstrahl die verkalkte Gallenblase als birnförmiger Schatten oder als Ringschatten erscheinen kann, ist im letzteren Fall eine Verwechslungsmöglichkeit mit einem Solitärstein oder einer verkalkten Cyste gegeben. So berichtet HERZ über einen Fall, der unter der Diagnose verkalkte Gallenblase operiert, sich als verkalkte Echinococcuscyste herausstellte, während umgekehrt GOLDHAMER den von TANDOJA beschriebenen Fall einer verkalkten Echinococcuscyste als verkalkte Gallenblase ansieht.

Ein verkalkter rechtsseitiger Psoasabszess kann ebenfalls ähnliche Bilder geben (Abb. 6). Bei dem abgebildeten Fall findet sich in der Gallenblasengegend ein scharfrandiger, intensiver Schatten mit fleckiger Struktur, der ganz genau dem Bild entspricht, welches die oben beschriebenen Porzellangallenblasen gegeben haben. Neben Aufnahmen in verschiedener Richtung und Berücksichtigung des Grundleidens an der Wirbelsäule kann die auffallend grosse Verschieblichkeit des Gallenblasenschattens bei Lagewechsel und Atemexkursionen, wie sie bei unseren zweiten Fall beschrieben wurde (vergl. Abb. 3 und 4) im Gegensatz zur konstanten Lage und eventuellen Doppelseitigkeit der Senkungsabszesse vor Täuschung schützen.

Zur Abklärung in zweifelhaften Fällen fordert ALBRECHT die Nachprüfung des Befundes mit Hilfe der Cholecystographie. Die Füllung der Gallenblase mit Kontrastmittel ist jedoch durch die Tatsache einer möglicherweise vorausgegangenen Entzündung a priori unwahrscheinlich gemacht, da nach durchgemachten Entzündungen durch Schleimhautproliferation, Adhäsion oder Schrumpfung der Ductus cysticus verlegt erscheint und der Auffüllung der Gallenblase naturgemäss im Wege steht.

Mehr Gelegenheit zu Verwechslungen mit andern in dieser Gegend vorkommenden Schattengebilden geben die Verkalkungen von mehr umschriebenem, inselförmigem Charakter. Da die Möglichkeit besteht, dass gelegentlich solche partiell verkalkte Stellen der Gallenblasenwand auf dem Röntgenbild zur Darstellung gelangen können, muss die differentialdiagnostische Überlegung auf diese Möglichkeit Rücksicht nehmen.

Gallensteine bieten in der Regel, wenn sie in den charakteristischen Ringschattenformen oder als zahlreiche fazettierte Schatten mit zentraler Aufhellung auftreten, keine Schwierigkeiten. Die Differentialdiagnose kann jedoch schwierig werden, wenn nur ein oder einzelne mehr oder weniger intensive, homogene Konkrementschatten sich abbilden.

Gegen die klinisch ebenfalls wichtigen Nierenkonkremente müssen Aufnahmen in verschiedener Projektionsrichtung, eventuell Pyelographie weiterhelfen. Weiterhin ist eventuell die Unterscheidung gegen Verkalkungen im Bereich des knorpeligen Rippenanteils der untern Apertur rechts erforderlich. Solche Kalkherde verlaufen jedoch in der Verlängerung der knöchernen Rippen und sind meist doppelseitig.

Unter Berücksichtigung der erwähnten differentialdiagnostischen Möglichkeiten ist also die Diagnose auf Porzellangallenblase einzig und allein anhand der dafür charakteristischen Röntgenbilder zu stellen. Diese Diagnose ist dadurch so wertvoll, dass sie vor Verwechslung des Röntgenbefundes mit Krankheiten in der Nachbarschaft der Gallenblase und mit Leiden, die röntgenologisch nicht in Erscheinung zu treten brauchen, schützen kann.

ZUSAMMENFASSUNG

Nach einer kurzen Einleitung über die pathologische Anatomie der kalkzifizierenden Gallenblasenwandentzündung beschreibt der Verfasser zwei Fälle von Porzellangallenblase, mit besonderer Berücksichtigung des charakteristischen Röntgenbildes. Er hebt die Wichtigkeit der Röntgenuntersuchung bei dieser seltenen Gallenblasenaffektion hervor.

SUMMARY

After an introductory discussion of the pathological anatomy of calcareous inflammation of the gall-bladder wall, the author reports two cases of porcelain gall-bladder. He pays particular attention to the characteristic röntgen picture and stresses the importance of the röntgen examination in cases of this rare affection of the gall-bladder.

RÉSUMÉ

Après une brève introduction sur l'anatomie pathologique des inflammations calcifiantes des parois de la vésicule biliaire, l'auteur communique deux cas de vésicule porcelanée, en tenant spécialement compte de l'image radiologique caractéristique de l'affection. Il signale l'importance de l'examen radiologique dans cette maladie rare de la vésicule biliaire.

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Abb. 1. Fall 1. Porzellangallenblase (Zielaufnahme).

= Nabelmarke

Abb. 3. Fall 2. Porzellangallenblase. Aufnahme v. d. (Querkolon z. T. mit Ba-Kontrastschatten).

Abb. 4. Fall 2. Aufnahme d. v. (Deutlicher Lagewechsel der Gallenblase gegenüber der Aufnahme Abb. 3).

Abb. 6. Verkalkter Senkungsabszess.

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FROM THE ROENTGENOLOGIC DEP'T OF THE STATE HOSPITAL, REYKJAVIK, ICELAND

ROENTGENOLOGIC CHARACTERISTICS OF ECHINOCOCCUS DISEASE IN BONES[1]

by

Gunnlaugur Claessen, M. D.

(Tabulæ XXXII—XXXIV)

In the present paper I publish a couple of new cases of roentgenologically examined echinococci in bones; but at the same time I wish briefly to review the problems which concern the radiologist in connexion with that disease. Its occurrence and various location in the skeletal system, as well as the pathoanatomical characteristics which distinguish it from parasitic cysts in other organs, are highly interesting. Knowledge of the particular pathoanatomical character of the cysts in the skeleton will aid the interpretation of the roentgenographic picture, and in making the diagnosis from other diseases. In the same manner, the roentgenogram may be helpful as guide for the mostly very doubtful prognosis, and of course the roentgen examination is important when it becomes a question of choosing the best operative procedure in cases of this very serious disease. Communications, in the literature, regarding roentgenologically ascertained parasitic cysts in bones are very few in number. The echinococcus in bones is an *avis rara*. If the picture of the roentgenology of the disease is to be made clearer, there is therefore good reason for dwelling in some detail on the few cases of it that happen to come under our observation.

Incidence and Localisation of Echinococci in Bones

In looking through journals on radiology one is impressed with the abundance of the literature to be found on the subject of cystic formations in bones. But with regard to *parasitic* cysts one not infrequently finds the remark: »will be mentioned, but not considered». The

[1] Submitted for publication Jan. 4th, 1934.

reason for this is perhaps that the echinococcus disease is found particularly in certain countries, and rarely in others. Yet the disease must be said to be a cosmopolitan one, inasmuch as sporadic cases occur everywhere. It is difficult to imagine that echinococci in bones should not be more or less frequent in such countries as Argentina, New-Zealand, Australia and Russia, even though communications to that effect are comparatively rare.

In my researches through the Icelandic medical literature preparatory to the publication, in 1928, of my monograph: »The Roentgen Diagnosis of Echinococcus Tumors» (Acta Rad., Suppl. VI), I found 8 cases, in all, of echinococci in bones; which is about 1 per cent. of all reported cases of echinococcus disease from Iceland, a country which has hitherto had the doubtful honor of being counted among the classic homes of the parasite. The ratio agrees fairly with what has been stated by other writers. The parasitic cysts in bones are usually reckoned as constituting 1.5 to 2 per cent. of all cases of echinococcus disease (LEHMANN, FRAENKEL, AKSELRAD).

It is by no means certain, though, that the localisation to the different bones is the same in all countries. In my monograph referred to above I was able to prove, as the result of roentgen examinations, that in Iceland, in contrast to what is the case in other echinococcus countries, the parasite is very rarely localised to the lungs. It was namely found that the cysts which had been diagnosed as echinococci of that organ were, as a matter of fact, subphrenic liver cysts with propagation and perforation to the lungs and bronchi. In the same way it is possible to imagine that there might be some geographical difference with regard to the cysts in bones; but as to that I do not believe any researches have been made so far.

The different incidence of echinococci in the various parts of the skeleton is a question of great interest. It is generally stated that in one third of all cases the localisation is to the bones of the pelvis. Next in order of frequency come localisations to the vertebral column, the femur, the tibia and the humerus. There is probably no part of the skeletal system in which the cysts have not been observed. The best conditions for their development seems to be where the cancellous substance is most abundant, as in the sacral and iliac bones. Their »preferred locations» during the early stage of the disease should, according to DEW, be the epiphyses and the parts nearest to these. Simultaneous occurrence in two bones is said to be very rare. It is found, however, in one of my own cases, reported farther on (no. I; G. S.).

The consensus of opinion seems to be that in about 30 per cent. of cases the echinococci lodge themselves in the bones of the pelvis. If this is correct, the total number of echinococcus cysts in bones recorded in the literature is very limited. Yet, in 1916, ROBIN gave a list of 122

known cases, and in 1924 DESPLAS and others had collected 43 cases of cysts in the pelvic bones alone. Since then, other cases have been reported by KIENBÖCK, FRAENKEL and GOLD, so that in 1931, according to AKSELRAD, the number of cases known, of echinococcus cysts in bones of the pelvis, had risen to 49. If we add to these the new case which I report in the present paper, the total number, up to the present, of cases with that localisation is 50, which should thus be one third of all cases of echinococcus cysts in bones. I do not believe, however, that it is possible from those figures to conclude anything very definite with regard to the aggregate number of echinococcus cysts in bones, because the statements in the literature are somewhat at variance. Still, they give an idea of how rarely this disease is diagnosticated.

As late as in 1933, KIENBÖCK has made an analysis of 86 cases from the world's literature, according to which the incidence of the cysts in different parts of the skeleton were as follows:

Extremities	26
Vertebral column	16
Sacrum	7
Bones of the pelvis	33
Various localisations . . .	4
	86

While the information with regard to the cysts in the bones of the pelvis tallies fairly well with what is known about the disease in the latter, the figures with regard to the other bones are less exact. In the present communication I describe also a new case of echinococcus in the fibula. In KIENBÖCK's recent study this localisation is not mentioned. It must thus be a rather unique phenomenon. ZIEGLER's case, which is mentioned by KIENBÖCK, cannot, in my opinion, be regarded as one of echinococcus in bone.

Beside the two new cases which I describe, I recapitulate in this paper the history of two others, already reported in my monograph of 1928 (Cases XLIII and XLIV). One of them — a case of echinococcus in the sacrum — I have had under continued observation since 1925. There have been several recurrences, necessitating repeated operations and roentgen examinations of the sacrum. The last of these roentgenograms, from May, 1933, is reproduced here, for comparison with the earlier pictures. The other case — an echinococcus in the femur, with spontaneous fracture — I reprint in order to have all my four cases of echinococci in bones recorded together in one place. I feel justified in doing so by the fact that it is extremely rare for one author to be able to publish, from his own observation, more than one case of echinococcus in bones.

Pathogenesis and pathoanatomical Features

It is to French authors, especially, that we owe our knowledge with regard to the pathogenesis of the parasitic cysts in bones and the resulting pathoanatomical changes in the latter. GANGOLPHE's work, from 1886, was for many years regarded as the classic description of those cysts. Most of his cases had already entered into a complicated stage, however, — with either infection or spontaneous fracture — which made it difficult clearly to discern the development of the parasite in the bone. It was therefore an event of great importance when, in 1916, the eminent authority on echinococci, DÉVÉ, succeeded in provoking echinococcosis experimentally in the bones of a rabbit, by injecting embryos of the parasite into the arteries of the animal. It now became possible to follow the development of the cyst in the bone from the very beginning. The pathoanatomical knowledge thus obtained became of great importance also for the interpretation of the changes in the roentgenologic picture. It now became evident that the action of the parasitic cysts in the bones is entirely different from their action in other organs.

The quite young cyst, lying in the medullary cavity, is roundish, clearly circumscribed, of benign appearance. But soon its shape becomes irregular, with numerous diverticular offshots (DEW), which begin to insinuate themselves into, and attack, the spongy substance. This is made possible by the fact that *in the bones the echinococcus is not, as in the other organs, surrounded by any strong, fibrous capsule.* In the other organs, this capsule, which is formed through reaction on the part of the host — for instance in the hepatic tissue closest to the parasite — has a considerable inhibitory effect on the development of the latter; but in the bones the conditions hardly exist for the formation of any such membrane of any strength. Besides, the mother sac is furnished with osteoclastic cells (DÉVÉ), which have a destructive influence on the osseous substance. The cyst is therefore capable of infiltrating the bone substance for a considerable distance, and spreads itself tortuously and in irregular shape between the osseous lamellæ.

In this manner, mechanical, ischemic and toxic actions combine to wear down and necrotise the spongy substance. The action on the cortical layer does not, as a rule, cause any great amount of expansion. The bone is destroyed by lacunar resorption. The process has the character of simple osteolysis, and as the periosteum usually remains inactive, spontaneous fractures often occur, and there is a great tendency to hematogenous infection and suppuration.

The process takes a long time, and the sick-history of the patients may extend over many years, or even decades. Parasitic cysts are usually

regarded as essentially benign; yet their growth in osseous substance certainly does not impress one in any way as such. Rather would one be inclined to place echinococcus cysts in bones somewhere intermedially between the benign and the malignant tumors.

As the cyst does not form any strong, fibrous capsule, there can be no expectation of finding any sharp morphologic limit for its extension in the osseous substance. This is an important fact, not only as regards the roentgenologic picture, but also from a surgical point of view, as attempts to remove the parasite radically by operation seldom succeed.

To a certain extent, the articulations form a barrier to the disease. This is the case, for instance, with the hip-joint; but in the latter the process can make its way around the joint, through the capsule (KIENBÖCK), and thus attack the femur, until the disease ends by spreading to the articulation itself (see Case I, farther on).

Case Journals

Case I. (922/31), G. S., farmer, aged 39 years. Had for a couple of years slight, intermittent pains in the region of the left hip. Claudication since the fall of 1930. In the early part of 1931 an intumescence as large as a closed fist was ascertained on the posterior aspect of the left iliac bone. The patient's physician made repeated punctures, with aspiration of pus and subsequent injection of iodoglycerine. The case was interpreted as surgical tuberculosis, and a course of light-baths was prescribed. There also came a smaller swelling in the inguinal region. Eventually, perforation occurred both there and on the back of the hip, and from the fistules issued tiny echinococcus sacs. This settled the diagnosis. In the latter part of July, 1931, the patient was admitted to the surgical department of the Reykjavik State Hospital. He was then very emaciated, and suffering from intense pain in the region of the left hip, localised particularly to the articulation itself, which was fixed in flexion and adduction. He could lie only on his right side. There were fistulæ in the regions mentioned, from which issued a few small sacs. *Clinical diagnosis:* Echinococcosis of the left coxa.

First roentgen examination, 29th July, 1931 (Fig. 1): Extensive destruction in left hip-joint. The caput practically obliterated. Incipient subluxation of the femur. The outlines of the acetabulum irregular and eroded. The joint cavity not effaced, indicating that the articular cartilage is partly preserved. Cavernous destructions in the entire left wing of the iliac bone, but with no visible connexion with the hip-joint. The iliosacral joint not affected. A conspicuous feature is the total absence of general osseous atrophy of the pelvis, in spite of the extensive destructions in the bones. Roentgenologic diagnosis: Echinococcosis of the left hip bone and femur.

Second roentgen examination, 5th August, 1931, after injection of lipiodol through the fistula in the left groin (Fig. 2): The contrast fluid seeks toward the left hip-joint, which proves that there has been perforation from the joint itself. In this film, which was taken with a somewhat shorter exposure time than the foregoing one, the entire iliac crest stands out clearly, showing a deep defectuosity in the uppermost part of the margin and lesser irregularities in a few other places. There are no periosteal neoformations.

Subsequent course: The leg was redressed, and extension bandage applied, whereupon the pain subsided considerably. By the middle of August, the fistula in the groin

healed spontaneously, while the one in the posterior side of the hip continued to suppurate, and from time to time discharged a single echinococcus sac.

Operation, 1st September, 1931, (Prof. G. THORODDSEN): Incision along the whole length of the left iliac crest, with following osteotomy of the ala ilii and echinococcotomy. The compact substance is well preserved, except for a couple of tracts opening into the fistula. The spongiosa, on the other hand, is reduced to a mushy detritus, completely destroyed by echinococci. In the course of the operation, the greater part of the external cortex is removed, and the interior scraped out, down toward the body of the bone. Lavage with formalin. Drainage. In the gluteal musculature is found an echinococcus the size of a hen's egg, which is extirpated.

Third roentgen examination, 9th September, 1931: Large defect resulting from operation (Fig. 3), comprising the greater part of the ala and extending down toward the acetabulum, the upper margin of which is noticeably smoothed out and little prominent. (It is not impossible that in the course of the operation some of the friable osseous tissue in the upper part of the acetabulum may have been scraped out). The subluxation of the femur more pronounced than before. The outlines of the collum quite sharp.

Subsequent courses: A few weeks after the operation an abscess close to the greater trochanter was incised, and was found to contain some echinococcus sacs. In March, 1932, the patient was discharged from the hospital. There was still at that time a fistula with very slight secretion in the cicatrix from the large operation, but for a long time there had been no passage of sacs. His general condition was good. He walked with the aid of crutches. During the summer he was able to help a little with the harvesting, but in August of the same year, according to letters received, he met with an accident, falling and sustaining a fracture in the region of his left knee-joint. As a result of this, he was confined to his bed for six weeks, but eventually got up again, and has not been seeking medical advice since.

Case II. (1992/32), H. B., workingman, aged 66 years. Grew up in the country, under unhygienic conditions. Among other things, great carelessness seems to have been shown in handling the dogs on the farm. For some thirty years he has had the feeling of a rather indolent intumescence in the upper part of his right leg. In 1926, he was operated on, in St. Joseph's Hospital in Reykjavik, for a cyst of the liver (echinococcotomy; Dr. HALLDÓR HANSEN, M. D.). Otherwise his health has been good until about two weeks ago, when the above named swelling in his right leg began to get intensily painful, and shortly after there came perforation, with issuance of pus and small cysts about the size of peas. He seems, on the whole, to be in a rather feeble condition. Owing to lymphangitis and edema the whole of his right leg is red and swollen, especially the lateral part, where there is the opening of a fistula, as large as the pulp of a finger. There is extensive fluctuation and suppurative exudation. After an incision had been made, on 10th March, 1932, and the pus evacuated, a firm intumescence could be felt in the upper part of the right fibula. *Clinical diagnosis:* Echinococcus in the right fibula, with abscess formation.

Roentgen examination, 15th March, 1932 (Fig. 4): For a distance of about 12 centimeters, the upper part of the diaphysis of the right fibula is cystically transformed, and so largely expanded that the bone is thicker than the diaphysis of the tibia. The cortex is as thin as paper, and with no new formation of periosteum underneath. The cavity is loculate. Upwards, the process is bounded by the former epiphyseal line; downwards, the limit of the cystic cavity is distinctly marked off against sound osseous tissue, with a cup-shaped widening of the diaphysis. Very little atrophy of the bone below the cystic part. *Roentgenologic diagnosis:* Echinococcus of the right fibula.

Operation, 16th March, 1932 (Dr. MATTH. EINARSSON, St. Joseph's Hospital): After a large subcutaneous abscess has been opened, a perforation through the muscles is dis-

closed. After the muscular layer has been penetrated, the distended portion of the fibula is encountered. In its anterior side is a lengthwise opening, several centimeters long. The bone is extremely thin, but the periosteum firmly attached. The upper portion of the fibula is resected below the cystic part. The cavity contained pus, detritus, and a few small cysts. It was not loculate; but in several places its walls were heavily ridged, which in the roentgenogram simulated septa.

Subsequent course: Owing to the infection, which had induced a septic condition, the patient failed to get better. There came a seropurulent accumulation in the knee-joint, which disappeared, however, after puncture and lavage with antiseptics; but nephritis supervened, with considerable albuminuria, and on 20th April, 1932, he died.

The photograph of the preparation from the operation (Fig. 5) shows the enormously distended bone, with a large defect in the wall of the latter. It may be noted that this defect does not show in the roentgenogram.

Case III[1]. (108/14), G. G., farmer, aged 58 years. While working in the field, in September, 1914, the patient fell heavily on his right hip, at the same time fracturing his left femur. Shortly after, he began to suffer greatly, with signs of phlegmonous inflammation at the point of the fracture, though the latter was not complicated.

Operation, in the beginning of October, 1914 (Dr. O. GUNNARSSON): Incision of a large abscess in the left thigh, on a level with the point of fracture. A great quantity of pus evacuated, together with a number of small echinococcus cysts. Drainage.

Roentgen examination, 14th October, 1914 (Fig. 6[2]): Transverse fracture of the left femur a few centimeters below the lesser trochanter, with considerable lateral dislocation. Signs of rarefaction and destructions in the structure of the diaphysis, as in a case of malignant tumor, and of thickening of the periosteum of the nether fragment. *Roentgen diagnosis:* Echinococcus in the diaphysis of the left femur; with fracture.

Subsequent course: The patient died from septicemia a few days after the operation. No post-mortem examination.

Comment: It would not have been possible from the roentgenogram to make a diagnosis of echinococcus in the bone, if the anamnesis had not supplied the information about cysts in the incised abscess. The latter must have been due to infection through the blood. Any other kind of malignant tumor would have given the same roentgenologic symptoms.

Case IV[3]. (806/18, 3497/25), K. J., carpenter, aged 27 years. For a long time before he was advised to seek the Clinic, this man had been suffering from pains in the small of his back, radiating into both thighs. For some time he had been treated for ischias, by the local physician. There was no deformity of his back, but considerable tenderness in the region of the sacrum, especially on palpation *per rectum*. No positive clinical symptoms of ischias. *Clinical diagnosis:* Osteitis of the sacrum (Ischias??).

Roentgen examination, 23rd July, 1918 (sent by Dr. J. KRISTJÁNSSON): Rather large cavity in the sacrum, occupying the middle portion of that bone (Fig. 7[4]). The sacral foramina are not seen as usual. *Roentgen diagnosis:* Cavities in the sacrum; presumably cyst (Tuberculosis? Malignant tumor?).

Operation, 2nd August, 1918 (Dr. MATTH. EINARSSON): After a preliminary puncture, which caused the outflow of some clear fluid containing echinococcus elements, echino-

[1] cf. Acta Rad., Suppl. VI, 1928; p. 76.
[2] = Fig. LXXX, Tab. XXIX in Acta Rad., Suppl. VI, 1928; p. 76.
[3] cf. Acta Rad., Suppl. VI, 1928; pp. 76—77.
[4] = Fig. LXXXI, Tab. XXX in Acta Rad., Suppl. VI, 1928: pp. 76—77.

Fig. 1. Case I.

Fig. 2. Case I.

Fig. 3. Case I.

Fig. 4. Case II.

Fig. 6. Case III.

Fig. 5. Case II.

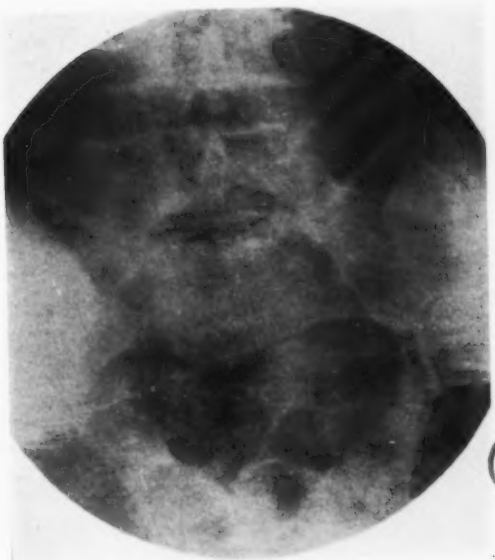

Fig. 7. Case IV.

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Fig. 8. Case IV.

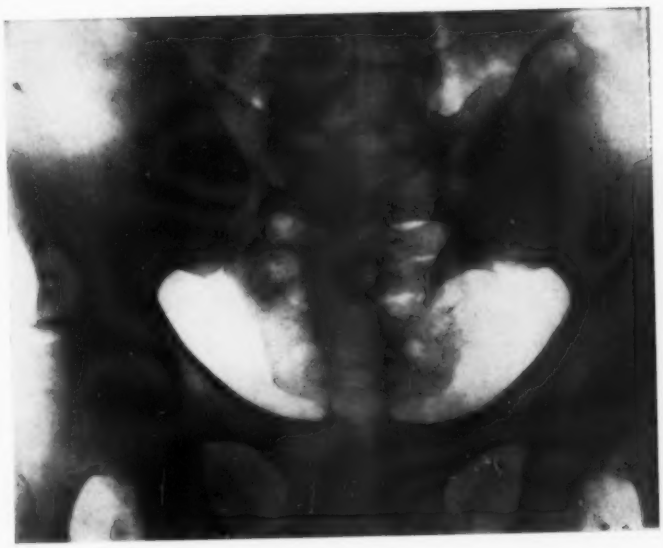

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Fig. 9. Case IV.

coccotomy was done, and a number of daughter-sacs removed from a cavity in the sacrum.

Subsequent course: There remained a fistula after the operation. Excochleation of the cavity was done a couple of times during the following years, the last time in April, 1920. The patient is able to work, and his general condition is good. There are no functional disturbances in the lower extremities. From time to time the fistula opens up, and a number of very small cysts come out. At our request, he presents himself at the clinic for renewed examination seven years after.

Roentgen examination, 18th October, 1925 (Fig. 8[1]): In the upper portion of the sacrum, to the left of the median line, is seen a sharply outlined, kidney-shaped defectuosity about six centimeters long, besides one or two smaller, roundish ones. The left margin of the bone, below the sacroiliac articulation, is uneven, with small defectuosities in the bone, and its structure atrophic. The upper margin of the sacrum is uneven.

Comment: A positive roentgen diagnosis is not possible in this case independently of the anamnesis and the clinical symptoms. Against tuberculosis spoke the fact that the patient was otherwise in sound health, and that there was no abscess in spite of the great extent of the destruction. Against a malignant tumor spoke the rather protracted course of the disease, the good general condition of the patient, and the circumstance that there was no palpable deformation of the bone. Against an echinococcus there could be no other argument than the fact that the lodgment of that parasite in the bony structure is very rare. In trying to account for the defectuosities in the bones, as seen in Fig. 8, the fact of the successive operative interventions must be borne in mind. . . . . .

Continued observation of the patient: As the patient continued to suffer periodically from sacralgia, swelling and tenderness around the fistula, the cavity in the sacrum was drained and disinfected three times during the years 1927—1928. In connexion with this, very slight osteotomies were done on the posterior side of the bone, but no excochleations. At the last of these operations only pus was found, but no cysts. Roentgen examinations in June, 1927, April 1928 and December, 1929, showed no essential changes from the former condition. In the course of 1932 fresh complications have set in, owing to irritation caused by the cysts to nervous factors in the patient's condition, retention of urine, difficult defecation and constrained walking. In March, 1930, a rather large cyst, projecting on the posterior aspect of the sacrum, from a cavity in the bone, was removed by echinococcotomy. The part of it which projected into the soft tissues was enclosed by a strong, fibrous capsule; the cavity of the bone was quite smooth, with a membrane covering the osseous substance. The cyst contained an immense number of daughter-sacs. A lump of adipose tissue was transplanted into the cavity. The operation wound healed. The same operative procedure was repeated in July, 1932, with healing as before. All operations were performed by Dr. MATTH. EINARSSON, of St. Joseph's Hospital.

At request, the patient presents himself in May, 1933. He is in a well nourished condition, but has been obliged to give up his work as a carpenter, and now earns his living as writer of topical songs and poems. He walks with some difficulty, owing to paretic weakness of his legs. Suffers from disordered urinary and rectal functions. Complete analgesia of the gluteal, anal and perineal regions; with frequent sacralgia, radiating downward into the extremities. On palpation *per rectum*, no defectousity is felt on the anterior aspect of the sacrum, nor any deformity of the bone. No fistula.

Roentgen examination, 24th May, 1933 (Fig. 9): In the left side of the sacrum, extending from the uppermost part of the latter to about the fourth sacral vertebra, there is an oblong cavity, or defectuosity, with smooth contours, as if the anterior or posterior

[1] = LXXXII, Tab. XXX in Acta Rad., Suppl. VI, 1928.

wall of the sacral canal had been removed. Besides, the osseous structure in the lateral part of the sacrum, below the sacroiliac joint, is pathologic, with partial destructions. Comparison with the roentgenogram taken six years before (Fig. 8) shows that the cavity is not nearly as sharply defined as formerly, and that the osseous process in the lateral part of the bone is now far more advanced. There is no question of any general atrophy.

Roentgen Diagnosis

When one first studies the roentgenograms of these four cases, the impression is that of a rather considerable diversity of the roentgenologic symptoms. The process in the iliac bone (Case I), and especially the one in the femur (Case III), impress one as malignant; while the cyst in the fibula (Case II) looks benign, and sharply marked off from the surrounding osseous tissue. In the last named case there is an enormous expansion of the bone, while in the femur there is no increase in the volume of the latter. At the first glance, these symptoms therefore appear rather chaotic and contradictory. A closer scrutiny nevertheless reveals certain *common features*, to which a not inconsiderable importance must be attached. Thus, there will be noticed, in all the cases, a *total absence of extensive regional atrophy of the bones*. The halisteresis is confined to the pathologic process itself, while the rest of the bone in which that process takes place is no more deficient in lime salts than normal. Another important feature is the *inactivity of the periosteum*. The pathologic processes may be characterised as a pure »tabula rasa» form of such, provoking hardly any reaction, or any apposition of freshly formed periosteum.

It is important to bear in mind these two concomitant features, — the absence of any regional atrophy of the bone, and of periosteal neoformations; because otherwise the roentgenologic picture is, of course, easily misinterpreted, owing to the rarity of the disease.

The errors most likely to be committed in that respect are that the echinococcosis in the bone may be mistaken for either (1) tuberculosis, (2) osteosarcoma, or (3) fibrous, cystic osteitis.

As regards the roentgenologic diagnosis from either of those diseases, in the cases described above, the possibility of *tuberculosis* might perhaps be thought to exist in cases I and IV. Let us, in the first of these, suppose that no perforation had taken place. Tuberculosis in the bones is invariably associated with extensive atrophy. Here we have an important mark of distinction from the parasitic cysts. With regard to the hip-joint in the same case (Fig. 1—3), we see that the cartilage is remarkably well preserved, at the same time as the osseous destruction is very extensive, — something which would be inconceivable in a case of tuberculous coxitis. If we add to this the amply calcareous structure of the mass of the iliac bone, farther down, nothing remains to support the supposition that the process should be of a tuberculous character. With regard to

Case I it has already been explained in the history of the case why there was no temptation to interpret it as one of tuberculosis.

It may be added that several authors have called attention to the fact that patients in whom echinococcosis has caused a remarkably large destruction of the hip-joint are nevertheless able to remain up and walking about, — something which is, of course, not the case with patients suffering from tuberculous coxitis. In most cases, the echinococci in the hip-joint are localised to the acetabulum, while the caput is not involved. The acetabulum may be completely destroyed without the latter being affected. Our case no. I is to a certain extent unique, since there the echinococcosis involved both the iliac bone and the femur. Otherwise, the occurrence of parasitic cysts simultaneously in two bones is, according to LEHMANN, very rare. KIENBÖCK describes a case of echinococcosis in the hip-joint with central, intrapelvic luxation of the caput through the totally destroyed acetabulum. The patient, a physician, was nevertheless able to be up and walk about, and even to support himself on the diseased leg alone! Such enormous, yet relatively indolent, destruction of bone reminds one of the *osteopathies of neurogenetic origin* (syringomyelia, tabes).

Sometimes the roentgenologic picture of echinococcosis in bone may easily be mistaken for one of *sarcoma* or *cancer*. The destruction of the bone as seen in Fig. 6 might be due to any kind of malignant tumor, and the extensive processes in the iliac bone in Fig 1, are not easily distinguishable from metastatic carcinosis. On the other hand, the appearance of the hip-joint, in the same picture, does not give the impression of malignancy. and as tuberculosis seems to be out of the question, one would rather be inclined to think of the destruction as being due to some neurogenetic cause or other. In Fig. 7, the cavity in the sacral bone, with its rather sharp demarcation, does not give the impression of a malignant tumor.

An interesting item of the differential diagnosis is the distinction of echinococcosis in the bones from *isolated, non-parasitic cysts* in the latter, and from *fibrous, cystic osteitis, either localised or in the generalised form known as Recklinghausen's disease*. Confusion with Recklinghausen's disease should be easily avoided, as the latter occurs in the form of multiple cysts separated by intervening areas of sound bone, while the echinococci occur so very rarely in two bones of the same individual that our case no. I must, as already said, be regarded as almost unique; and of generalised echinococcosis no case has ever been observed, according to LEHMANN.

A far more difficult problem is the distinction of echinococcosis in the bones from those cystic formations which one observes in cases of localised fibrous, cystic osteitis, whose growth is often expansive from the centrum outwards, and where the cortex is thin as paper, and the

cavity divided by septa, in the same manner as, for instance, in the fibula in our case no. II (Fig. 4). In such cases, the diagnosis from echinococcosis will often be impossible.

With regard to the *expansive growth, from the centrum outwards*, it might be wondered why it is so considerable in the fibula in case no II (Fig. 4), while in the femur in case III (Fig. 6) there is hardly any increase in the volume of the bone. Of course, the possibility for expansion exists from the moment when the parasite has destroyed the spongy tissue and corroded the cortex. In a bone like the fibula, which is not called upon to bear any considerable part of the weight of the body, the increase in volume can continue until the walls are as thin as paper; but in the femur, which has to bear a far greater weight, nothing similar will be possible, for the simple reason that the bone will become fractured long before the destruction of the cortex and the resulting expansion have reached such a degree. Also in the tibia, an expansion similar to the one in the fibula would be unthinkable, because also there the weight of the body would certainly cause spontaneous fracture at a much earlier stage. In certain cases of osteosarcoma, the mass of the tumor is able to sustain a considerable weight, but the same is not the case with bones that have been invaded throughout by a parasitic cyst. In interpreting the roentgenologic symptom of central expansion it is therefore necessary to consider in which of the bones of the skeletal system the affection resides, — a point which I have not found stressed anywhere in the literature on this subject.

Another feature of the roentgenogram of the fibula in case II (Fig. 4) which calls for attention is the appearance of the cavity as being loculate, while at the operation no septæ were found, but only some slight, elevated ridges on its inner side. The septæ have undoubtedly existed at an earlier stage, but have been destroyed in the already far advanced process of degeneration and infection, until, at the time when the roentgenogram was taken, only traces of the thickened bases from which they arose were left. According to REINBERG, the loculate appearance of the cavity is the characteristic by which other diseases may be positively distinguished from a *chronic abscess in the bone* (*Brodie's abscess*). In cases of the latter there is osteosclerosis of the surrounding bone, and, besides, 75 per cent of such cases are localised to the tibia.

The roentgenologic diagnosis of echinococcosis in the bones is by no means easy, not least because the disease is so rare. But in those countries where echinococcosis is endemic it should nevertheless not be so that the roentgenologic diagnosis of the cysts is possible only after operation or spontaneous rupture.

The Importance of the Roentgen Examination as Basis for the Prognosis and Treatment

The chief fact in these respects is the circumstance that in the bones the echinococcus is not surrounded by a fibrous capsule sufficiently strong to keep the cyst within bounds and prevent it from spreading. In the other organs, the fibrous capsule acts as an efficient barrier, which marks the extent of the cystic growth. In the liver, a calcified capsule will show one the outside limits of the cyst; in the bones they cannot in any way be determined roentgenologically.

The theories advanced by DÉVÉ and others to account for the absence of any capsule around the parasite in the bones do not stand the test of experience. As the record of the operations in our case no. IV showed, Dr. EINARSSON, on one of those occasions, found the cysts imbedded in a smooth cavity covered with a membrane which changed immediately into a strong capsule over those parts of the cyst which projected into the soft tissues. Theoretically, there is nothing to prevent the formation of a capsule in the bone. Both connective tissue and blood vessels are present, from which a membrane might be built up. As a matter of fact, DEW speaks of a cellular membrane surrounding the parasites. But whether, theoretically, such a membrane exists or not, it is, at any rate, not sufficiently strong to offer any appreciable resistance to the spread of the cystic growth. As already mentioned, the spongy tissue becomes infiltrated and worn down, usually without any definite limits of the process being observable; as may be seen in our cases I, III and IV. The spread of the disease in the osseous tissue often resembles that of a malignant tumor. It is not only in the roentgenogram that it is difficult to determine the limits of this spread. Even for the surgeon who does an autopsia in vivo it is impossible to be sure whether an attempted excochleation has, after all, been absolutely radical. Unfortunately, the disease almost invariably recurs.

There are exceptions to every rule, however. In Fig. 4, one really has the impression of a definite, clearly marked limit to the extent of the tumor downward, with a sudden transition from diseased to sound osseous tissue; an impression which was fully confirmed by the subsequent operation. As a general rule, it must be said, however, that the roentgenologist should be very careful about expressing any opinion with regard to the extent of the echinococcosis in the bone.

SUMMARY

On the basis of 4 cases the author describes the roentgen findings in parasitic bone cysts.

Cases of echinoccosis in bones constitute from 1 to 2 per cent of all cases of echinococcus disease. The localisation is most often to the bones of the pelvis, but there is hardly any part of the skeletal system in which the cysts have not been observed.

The cases observed by the author comprise echinococci in the iliac bone, the head of the femur, the sacrum, the diaphysis of the femur, and the fibula.

The echinococcus infiltrates the spongy substance, in most cases without any visible morphologic limit to its spread, and attacks the cortex. The cases are frequently complicated by infection, suppuration and spontaneous fracture.

The destructions in some cases may resemble any kind of malignant tumor, while, in other cases, they are of a more benign character. An important pointer for the roentgenologic diagnosis is the absence of any regional atrophy of the bone, and of any reaction on the part of the periosteum. The author discusses in detail the diagnosis of the parasitic cysts in the bones from such diseases as surgical tuberculosis, osteosarcoma and fibrous, cystic osteitis.

The limits of the echinococcus in the bone can very rarely be determined with certainty from the roentgenograms.

ZUSAMMENFASSUNG

Verf. beschreibt auf Grundlage von 4 Fällen die Röntgenbefunde bei parasitischen Knochenzysten.

Die Fälle von Echinoccocosis in Knochen machen 1—2 % aller Fälle der Echinokokkuskrankheit aus. Die häufigste Lokalisation sind die Beckenknochen, es gibt aber kaum irgendeinen Teil des Skelettsystems, in welchem diese Zysten nich beobachtet worden sind.

Die vom Verf. beobachteten Fälle betrafen Echinococci im Darmbein, im Femurkopf, im Sakrum, in der Femurdiaphyse und der Fibula.

Der Echinokokkus infiltriert die spongiöse Substanz, in den meisten Fällen ohne sichtbare morphologische Grenze seiner Ausbreitung, und greift den Kortex an. Die Fälle sind häufig durch Infektion, Suppuration und Spontanfraktur kompliziert.

Die Zerstörungen können in manchen Fällen jeder Art von malignen Tumoren ähneln, während sie in anderen Fällen von mehr gutartigem Charakter sind. Ein wichtiger Fingerzeig für die röntgenologische Diagnose ist das Nichtvorhandensein jeder regionären Knochenatrophie und jeglicher Reaktion vom Periost. Verf. erörtert im Detail die Diagnose der parasitären Knochenzysten gegen Leiden wie chirurgische Tuberkulose, Osteosarkom und fibröse zystische Osteitis.

Die Grenzen des Echinokokkus in Knochen können durch Röntgenogramme sehr selten mit Sicherheit bestimmt werden.

RÉSUMÉ

L'auteur décrit, en s'appuyant sur 4 observations, les constatations radiologiques dans les kystes parasitaires des os.

Les cas de kystes hydatiques constituent de 1 à 2 % de toutes les affections échinococciques. La localisation la plus fréquente est le squelette du bassin, mais il n'y a presque pas un os dans lequel on n'ait observé de kyste hydatique.

Les cas constatés par l'auteur siégeaient dans l'os iliaque, la tête du fémur, le sacrum, la diaphyse fémorale et le péroné.

Les kystes hydatiques infiltrent le tissu spongieux, dans la plupart des cas sans limite morphologique visible de leur invasion, et attaquent l'écorce. Ces cas s'accompagnent fréquemment d'infection, de suppuration et de fractures spontanées.

La destruction donne parfois l'impression d'une tumeur maligne, tandis que, dans d'autres cas, elle est d'allure plus bénigne. Une particularité qui a son importance au point de vue du diagnostic radiologique, est l'absence de toute atrophie régionale de l'os et de toute réaction périostique. L'auteur discute le diagnostic différentiel des kystes parasitaires des os et de certaines autres affections telles que la tuberculose chirurgicale, l'ostéo-sarcome et les ostéites fibreuses kystiques.

Il est rare que les limites de l'échinocoque puissent être établies avec certitude par la radiographie.

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